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COVER: One case of Japanese quinine tablets that will never reach enemy troops is shown being examined at the American Institute of Pharmacy, Washington, D. C. The seal used on the bottles indicates that this antimalarial ammunition has been extracted from the richly-bearing cinchona bark of Java, a source formerly available to the United States.

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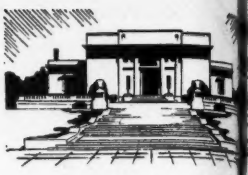


The Way I

EXCLUSIVE use of the metric system for doses in the Pharmacopœia and National Formulary seems to be in order now that the A. M. A.'s Council on Pharmacy and Chemistry has limited expressions of weight and measure to the metric system in its publications and further encouraged conversion by suggesting that the system be adopted by medical schools and pharmaceutical manufacturing laboratories.

This action is the outgrowth of a trend that has been developing for decades and not a hasty or revolutionary step. The gram and liter have had the full weight of scientific opinion fighting on their side and have won hands down in the professions, excepting pharmacy and medicine. Use of the apothecaries' system is rooted deep in the history of the pharmacist and physician, however. Particularly in the field of prescription writing the drachm and fluid ounce still seem to hold an edge over their metric counterparts, although their lead has been steadily narrowing.

Metric Millenium?

This situation has added to the confusion and danger inherent in the use of two systems. It is to the credit of pharmacists, perhaps more than to the physicians, that patients have been subjected to so few mistakes in medication. The inevitable serious accidents in dosage that have occurred, however, are given by the Council on Pharmacy and Chemistry as the immediate, practical stimulus for its ban on the use of the apothecaries' system in its publications.

Marked effect on prescription writing habits should result from this move, for it includes such widely used physicians' handbooks as the *Epitome of the U. S. Pharmacopœia and National Formulary, New and Non-Official Remedies, Useful Drugs,* and *Interns' Manual.*

The initiative in adopting the metric system has lain with medicine. For by the very nature of the pharmacist-physician relationship it has been the pharmacist's function to dispense medications on the order of the physician, within legal bounds, no matter how the prescription may be written. It is always the pharmacist's hope (not always fulfilled) that the physician will express himself in a mutually intelligible language.

Certainly the promotion of the metric system is a step in the direction of clarity and accuracy that should be welcomed by pharmacists in these days of more potent and therefore more dangerous drugs.

Most of us in pharmacy have a sentimental attachment to the apothecaries' system because it represents an ancient tradition and an esoteric part of the profession. Little more can be said for it. As pharmacy advances with the other professions, it is only natural that metric weights and measures should supersede more confusing expressions, such as the three different kinds of ounces now used.

The metric system, originating in France, is based entirely on $^1/_{10,000,000}$ of the earth's quadrant, the distance from the equator to the pole. Thus the meter was derived as the basic unit of length. For the unit of volume the cube of the decimeter was designated as a liter. The gram, basic unit of weight, was defined as the weight of 1 cc. of distilled water at 4° C. All other denominations of these three units were evolved on a decimal basis. For simplicity and rationality the system would be difficult to improve upon.

The official compendia have adopted it for formulas, assays and other parts of the monographs until only the vestigial apothecaries' doses remain as alternate approximations for the metric quantitities given. Dele-

Looks To Us

tion of the apothecaries' doses is the next logical step. The transition period could be bridged by including detailed conversion tables in a prominent place in the U. S. P. and N. F. Such a move would eventually put the dispensing of medications—where precision and clarity are paramount—on a more rational basis.

Better Prescription Writing

TEACHING pharmacy to medical students would not seem to be of particular benefit to the practicing pharmacist at first glance. From behind the prescription counter it might not even look like a good idea, just as pharmacology for pharmacy students looked like the primrose path to counter prescribing to the physician at one time. A little knowledge may still be a dangerous thing but to the competent physician and pharmacist a better understanding of the other's work will form a basis for fuller coöperation and a greater realization of the need for both in providing optimum medical care.

America's medical schools, on the average, are the best in the world. Yet it is recognized by pharmacists and physicians alike that after the young medical graduate makes an expert diagnosis and decides on the rationale of treatment, he is usually not fully prepared to make use of the advantages that well-written, individualized prescriptions can give.

Many questions may arise in the mind of the young physician. Which vehicle? Is it soluble? Incompatible? After all it is much easier to write the name of a standardized product from a commercial laboratory. Pharmacists can do much to aid physicians in utilizing pharmaceutical resources by diplomatic coöperation. A more basic approach is better instruction in prescription writing in the medical schools.

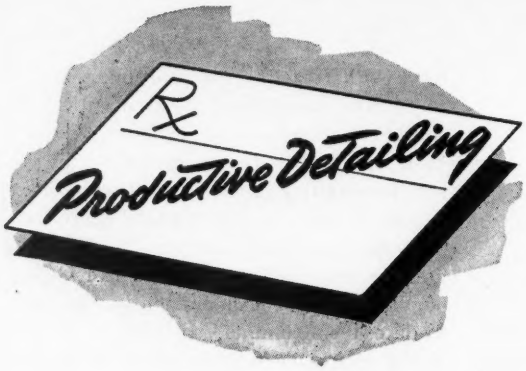
This problem is not new and there have been many attempts to solve it. The progressive plan used at the Medical College of Virginia has been eminently successful to date, if not unique. In brief, a member of the pharmacy school faculty walks into the pharmacology class of medical students once each week to discuss with them the writing of prescriptions for the material studied. Other mutual problems, such as the intricacies of narcotic laws, are reviewed.

To us, the logic of this procedure is summed up by Dr. Harvey B. Haag, head of the M. C. V. department of pharmacology, when he writes in *The Virginia Pharmacist:* "A prescription is a message from a physician to a pharmacist, and so the better these two understand one another the more smoothly will this message be interpreted and executed."

Although it is too early for the medical faculty to put a final evaluation on the results obtained, Dr. Haag reports that it has been sufficiently successful to warrant an extension of the coöperative plan.

A program similar to the one at Virginia can be inaugurated wherever a pharmacy college and medical college are operating in the same area and further extended to include dental, nursing and veterinary schools.

Nor need the plan be a one-way street. Pharmacy students could gain much from exchange lecturers in these fields. Too often, even in our universities, each professional college operates as a self-contained unit. The young practitioner then finds himself a stranger when coöperating with the allied professions. Wherever pharmaceutical educators can adopt the coöperative plan of the Medical College of Virginia, the reward be more rational medication and increased professional practice for the pharmacist.



Some Modified FORMULAS FRM

COMMITTEE ON PROFESSIONAL RELATIONS PRESENTS ANOTHER PROJECT IN ITS PRODUCTIVE DETAILING SERIES; IMPROVE YOUR SERVICE TO PHYSICIANS BY INDIVIDUALIZED FORMULAS

SIMPLE Ointment, U. S. P., has been widely used for decades as a standardized base. In U. S. P. XII the official name was changed to White Ointment, and a similar base, made with yellow wax and petrolatum instead of the white grades, became official as Yellow Ointment. This ubiquitous pair provide readily available bases for a number of official products, but because of their official status they are often used by the physician without regard for the niceties of prescription writing.

More individualized formulas which take into account the level of activity desired—*i. e.*, epidermic, endodermic or diadermic—are suggested by Dr. Herman Goodman, New York dermatologist and author of *Rational Pharmaceutical Treatment of Skin diseases.* In *Archives of Dermatology and Syphilology* (49:1, 1944), he points out that the predominance of mineral grease in the official bases lessens their value for the treatment of skin or scalp disorders when there is oozing or moisture present.

A pharmaceutical problem sometimes posed by use of the official bases is the difficulty of incorporating powders. In alternative formulas given below, the liquid petrolatum permits the pharmacist to moisten powdered ingredients of a prescription, thereby facilitating the compounding of an elegant ointment.

If the physician wishes to prescribe an ointment only for its action on the outermost layers of the skin (epidermic), Dr. Goodman suggests the following base:

	Gm. or cc.
Light liquid petrolatum	5
Wool fat	5
White petrolatum, to make	100

Where endodermic action is desired, different drugs present different problems. In general, however, it has been recognized that petrolatum is a very poor vehicle for medicatjon intended to reach the lower skin layers. Although wool fat stands between petrolatum and lard in its ability to penetrate the skin, it has the added advantage of not becoming rancid. For prescriptions intended to have an endodermic level of action, Dr. Goodman therefore suggests a base with reduced mineral grease content:

	Gm. or cc.
Light liquid petrolatum	5
Wool fat	30
White petrolatum	100

In using formulas of this type physicians may order water, as necessary, to dissolve water-soluble ingredients. A recommended formula for endodermic ointment of boric acid contains:

	Gm. or cc.
Boric acid, in fine powder	10
Water, to moisten	10
Wool fat	30
White petrolatum, to make	100

Using a modification of this formula as a base, Dr. Goodman proposes the following formula for the treatment of hyperkeratotic lesions of ringworm of the toes and toe interspaces, which are characterized by horny growths and usually seen in cases of long duration:

FRMATOTHERAPY

	Gm. or cc.
Salicylic acid	6
Light liquid petrolatum	5
Wool fat	12
White petrolatum	100

This formula is intended as a substitute for Ointment of Benzoic and Salicylic Acid, N. F. (Whitfield's ointment). Dr. Goodman sees no good reason for including benzoic acid in a prescription used for treating ringworm of the toes and toe interspaces.

"One who prescribes the ointment," he writes, "desires either keratoplastic action or keratolytic action. A made-to-measure prescription designed for the individual patient can be written. The patient is assured of the needed action by selection of the proper concentration of the chemical reducing agent, salicylic acid."

Experiments have indicated that certain volatile drugs are useful in prescriptions of this type to inhibit the growth of the tinea organisms. Depending on the preference of the physician, any of the following drugs can be incorporated into the salicylic acid ointment formula in a total strength of not more than 2%: thymol, chloral hydrate, menthol and camphor.

An alternate formula for hyperkeratotic lesions of ringworm of the toes can be prepared as follows:

	Gm. or cc.
Chrysarobin	5
Chloroform, to make	100

In cases with denudation of the skin, Dr. Goodman points out that salicylic acid's keratolytic action, which separates the horny layer, is not necessary. Instead he prescribes antiseptic drugs, preferably in the form of a liquid. A typical preparation for denuded lesions of ringworm of the toes and toe interspaces contains:

	cc.
Tincture of aconite, N. F.	20
Tincture of iodine	30
Alcohol, to make	100

ABSORBENT POWER of Lassar's plain zinc paste is improved by changing the formula to include cetyl alcohol.

Since the avoidance of reinfection is an important part of the therapeutic regimen, the following preventive powder is prescribed:

	Gm.
Phenyl salicylate	1
Chloral hydrate	1
Sterilized purified siliceous earth, to make	100

Turning from the discussion of alternate formulas for Whitfield's ointment, Dr. Goodman suggests to the prescribing physician modifications of Paste of Zinc Oxide, N. F. (Lassar's plain zinc paste). Maintaining that the official preparation is difficult to apply and more difficult to remove, particularly from hairy parts, he recommends the use of boiled starch instead of starch. The resulting product is easier to apply and to remove and has the desired action on the skin. A second change in the formula substitutes an animal fat, such as lard or benzoinated lard, for the white petrolatum in the official product. The natural emulsifying fraction of the fat permits better absorption of exudates due to cutaneous irritation. The formula as given will provide a medium for mold growth and thus should be prescribed for immediate use.

	Gm. or cc.
Starch	25
Water	50
(Rub starch in cold water until smooth; heat and stir until translucent)	
Zinc oxide	25
Lard, or benzoinated lard	50

Poor Absorbent

This is not the first time that a modification of the official paste has been suggested. Although Lassar's plain zinc paste has been almost indispensable in the practice of dermatology, physicians have long been dissatisfied with its absorbent qualities. Every ingredient of the original formula, with the exception of zinc oxide, has been replaced by investigators at one time or other.

Two decades ago, the German dermatologist, P. G. Unna, also suggested the use of benzoinated lard in the paste to increase its drying power. Lassar, himself, realized that fats are impermeable to serum or water, but argued that the paste could take up serous exudates by capillary action of the solid constituents. The work of various investigators has failed to verify this supposition. Lassar's theory is further exploded in *Archives of Dermatology and Syphilology* by a report from Dr. Ernest A. Strakosch of the Division of Dermatology and Syphilology, University of Minnesota.

Zinc oxide as well as starch (or talc) is surrounded by petrolatum and therefore cannot come into direct contact with the serum or sweat. How, then, asks Dr. Strakosch, can they act like filter paper, as suggested, by taking up the serum from the skin and giving it up by evaporation from the surface?

After summarizing the work of other experimenters, he concludes that it has been satisfactorily shown that zinc oxide paste of the Lassar type is unable to absorb water or serum. Taking the problem into the laboratory, Dr. Strakosch confirmed that a hydrocarbon base, such as petrolatum, does not take up watery fluids. His experiments also showed that the addition of emulsifiers or—instead of petrolatum—the use of emulsion bases would provide water-absorbing pastes. This apparently demonstrates that the process is based on emulsification, rather than on capillary action as Lassar believed.

In compounding the test preparations, water-free ingredients were used. Then desiccated cobalt chloride, which turns from blue to pink in the presence of water, was added as an indicator. Four hours after application of the pastes to the forearm of a test subject, color comparisons were made.

Under these conditions hydrous wool fat—usually a good emulsifier—gave disappointing results. Another interesting point demonstrated was that starch-containing pastes always showed a better absorbing power than those containing talc, which has replaced starch in formulas of this type from time to time. (Aside from this fact, talc has also been accused of causing irritations.)

On the basis of the data obtained, the following formulas with emulsion bases proved most satisfactory:

	Gm.
Zinc oxide	7.5
Starch	7.5
Cetyl alcohol	1.5
Petrolatum, to make	30

Zinc oxide	7.5
Starch	7.5
Fatty acid esters of diethanolamine with petrolatum,[1] to make	30
Zinc oxide	7.5
Starch	7.5
Oxycholesterol-petrolatum base,[2] to make	30

Formulas discussed here—the ointment bases, the tinea preparations, the modified zinc pastes—were suggested by specialists in a leading dermatological journal, but they are types of preparations which are often used by the physicians of your community. The formulas can be *individualized* to suit the needs of the patient and the preferences of the physician, a point which best exemplifies the advantage of coöperation between pharmacist and prescriber.

The Committee on Professional Relations of the AMERICAN PHARMACEUTICAL ASSOCIATION presents this material as a part of its program to give pharmacists the opportunity to extend their professional services. Many general practitioners will not have an opportunity to read the original papers in which these formulas were presented. Make up sample prescriptions and detail physicians on those which you believe will be of most interest to them.

[1] Available as Hydrosorb from Abbott Laboratories, North Chicago, Ill.

[2] Available as Aquaphor from Duke Laboratories, Stamford, Conn.

NEW ALCOHOL TAX LAW NOW IN EFFECT

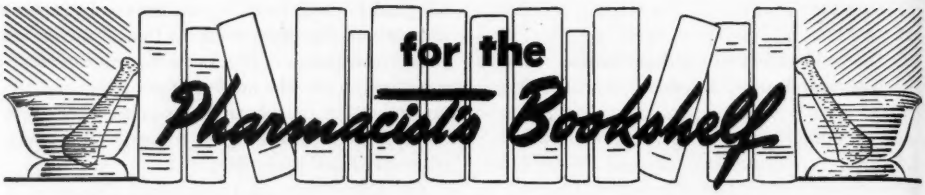
ALCOHOL tax drawback for pharmacists is simplified and increased by the new revenue act passed by Congress. The rebate is raised to $6 from the old rate of $3.75 per proof gallon and can be claimed at any time during the three months following the quarter in which the alcohol is used to make nonbeverage products. It is no longer necessary to wait until the products are sold before claiming the drawbacks. The tax itself has been increased to $9.00 from $6.00 per proof gallon, thus increasing the net tax after drawback by $0.75 over last year. Pharmaceutical manufacturers will not be permitted to raise ceiling prices, however, on products manufactured with ethyl alcohol above those prices originally established at the March, 1942, level under the General Maximum Price Regulation. This is because the present tax will be a lower cost factor than the $4.00 tax with no drawback that was then in effect. Where prices were reduced after the drawback provision was made, prices may be increased to the original maximum price level.

As in the past, pharmacists must pay a special tax of from $25 to $100 (depending upon the amount of distilled spirits used) to become eligible for the drawback. For those using less than 25 proof gallons of distilled spirits annually, up to $150 rebate can be obtained at a cost of $25 for the special tax; the use of only 4.17 proof gallons per year is required to equalize the special tax. For those using between 25 and 50 proof gallons, however, the special tax is $50, and $100 for more than 50 proof gallons.

Information and supporting data on how the alcohol was obtained and used must be filed with drawback claims as outlined in the material being supplied to all taxpayers by the Bureau of Internal Revenue.

Alcohol on hand April 1 when the new law went into effect is subject to a floor stocks tax of $3.00 per proof gallon. Alcohol that is in the process of manufacture on April 1 and has lost its identity as distilled spirits is eligible for the former drawback of $3.75 per proof gallon.

Pharmacists planning to claim the drawback must prepare an inventory dated as of April 1, showing separately the amounts of distilled spirits, unfinished products, finished products, recovered distilled spirits and intermediates containing distilled spirits. Duplicate copies should be forwarded at once to the supervisor of the Alcohol Tax Unit for the Internal Revenue District in which the laboratory is located; a third copy of the inventory must be retained by the manufacturer.



RECENT books and brochures of interest to pharmacists are listed below for the convenience of our readers. As an additional service, the PRACTICAL PHARMACY EDITION will obtain books for you or supply additional information. If there is a book related to the practice of pharmacy that you are unable to secure, THIS JOURNAL will send it to you postpaid upon receipt of check or money order covering the retail price.

SUPPLEMENT TO NEW AND NONOFFICIAL REMEDIES 1943—*American Medical Association*, 535 N. Dearborn St., Chicago, 44 pp.; without cost to those who have purchased NNR. Contains descriptions of drugs that have been accepted by Council on Pharmacy and Chemistry since 1943 edition was published. For convenience of NNR users, a permanent subscription list has been set up. Those requesting to be put on list are sent new editions and supplements as published, and subscriber is billed at $1.50 per year.

CLINICAL GUIDES TO SEX HORMONE THERAPY—*Medical Research Division, Schering Corp.*, 86 Orange St., Bloomfield, N. J., 158 pp., illus.; free to pharmacists and physicians on request. Three booklets, attractively bound and boxed, covering female sex hormones (follicular and corpus luteum) and male sex hormone (testosterone). Promotional aspect subordinated to apparently sound discussion of physiology, chemistry and therapeutics of sex hormones. Of use to pharmacists as background for intelligent coöperation with physicians. Bibliographies are included for those wishing to explore the literature for extensive information.

HENLEY'S TWENTIETH CENTURY BOOK OF TEN THOUSAND FORMULAS, PROCESSES AND TRADE SECRETS—*Norman W. Henley Publishing Co.*, 861 pp., $4.00. Promoted for use in the professions but primarily designed for the amateur. Encourages the laity to compound pharmaceutical preparations, many of them of questionable rationale. Some journals listed as "authorities consulted" are no longer being published. Because of the volume's wide scope it is a handy reference for certain household and workshop formulas.

EPITOME OF THE PHARMACOPOEIA AND NATIONAL FORMULARY—*American Medical Association*, 271 pp., $0.60. Gives condensed description of each drug, its preparations, and the dose, action and use of each. Particularly useful as handbook for physicians.

20 YEARS OF MEDICAL RESEARCH—Dorothy White Nicolson—*National Tuberculosis Assoc.*, 94 pp., $0.50. A readable review of plans and achievements of the Committee on Medical Research of the National Tuberculosis Association coöperating with other research agencies.

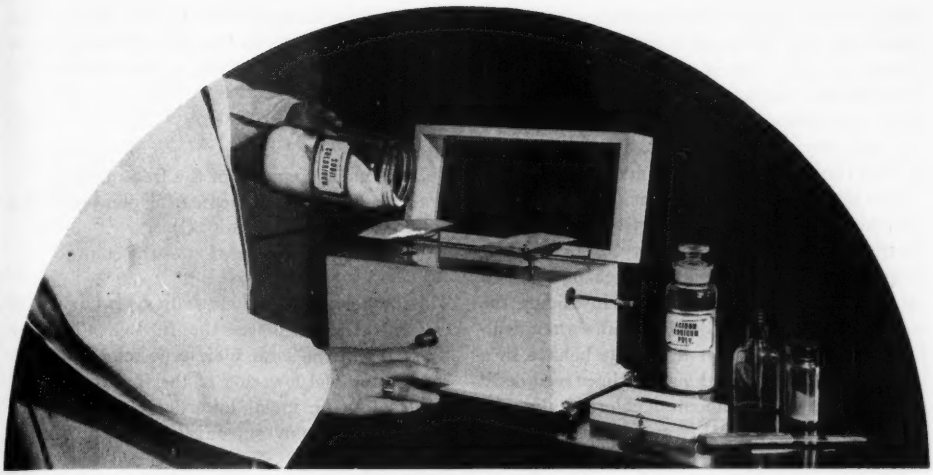
FIRST BOUND SUPPLEMENT TO U. S. PHARMACOPŒIA XII—*Pharmacopœial Convention*, 104 pp.; sent on receipt of order card attached to back cover of U. S. P. XII.

THIRD AND FOURTH SUPPLEMENTS TO NATIONAL FORMULARY VII—*American Pharmaceutical Association*, 10 pp. and 1 p.; send large stamped envelope with request to Justin L. Powers, chairman, Committee on National Formulary, 2215 Constitution Ave., Washington 7, D. C.

A TREATISE ON BENZOATES—*Seydel Chemical Co.*, Jersey City 2, N. J., 21 pp., free on request. Small commercial pamphlet reviewing history of benzoates as drug and food preservatives and summarizing uses and regulatory laws.

HEALTH OF CHILDREN IN OCCUPIED EUROPE—*International Labour Office*, Montreal, 37 pp. $0.25.

VITAMIN REVIEWS—*Merck & Co.*, Rahway, N. J., 59 pp., illus.; available to pharmacists and physicians without cost. Five pamphlets in slip cover containing concise information on description and properties, occurrence, requirements, dosage and clinical use of vitamins.



Rapid Method for CALCULATING ISOTONIC SOLUTIONS

by JULIAN M. WELLS

COLLEGE OF PHARMACY, UNIVERSITY OF CALIFORNIA

IN THIS COMPREHENSIVE STUDY OF ISOTONICITY, PHARMACISTS ARE GIVEN A PRACTICAL METHOD FOR MAKING CALCULATIONS THAT SOLVES A RECURRING PROBLEM

MANY methods[1–11] have been propounded for calculating the amount of a substance required to prepare a solution isotonic with various body fluids. While these methods are suitable for calculating isotonic solutions their practical application by the pharmacist is often limited. Certain methods can only be used for single ingredients, others for only specific types of substances. Some involve the use of algebraic equations. Some require long and tedious calculations which must be repeated for each ingredient used. In others, essential data are not always easily obtained, especially for new substances. In a few cases the accuracy of results must be questioned.

For these reasons the method being described was developed to provide a simple, practical system suitable for general work. It has been used and tested for several years, both for teaching purposes and in prescription practice. A recently published paper[12] describes the method in detail. The present paper will briefly review the basis for development of the method and present the essential equations and tables for use in the pharmacy. While the several equations and tables as shown might suggest another complicated, impractical method, such is not the case. In practical prescription work only one table (Table II) is necessary, plus the ability to multiply, add and subtract.

For most practical purposes one solution is isotonic with another if the two solutions have the same freezing point. The freezing point of blood serum is about $-0.56°$ C. If the molal lowering of the freezing point is known for aqueous solutions, it is possible to calculate the molal concentration of a particular substance required for isotonicity. This is true if the membrane involved is truly semipermeable, that is, permeable to the solvent and not to the solute. The membranes found in the mammalian organism are permeable to some solutes, and impermeable to

others. For example, the membrane that surrounds the red blood cell is impermeable to the plasma proteins, but is permeable to urea and other blood constituents. Based on freezing-point comparisons these exceptions to the general rule may not be apparent, but they are evident in terms of physiological action.

It is known that certain chemicals do not prevent hemolytic action, irrespective of their concentration in terms of isotonicity. The peculiar properties of these chemicals, which make them exceptions to the rule, in no way invalidate the accuracy of this method or its results when dealing with the many chemicals that behave in a normal manner. Exceptions have been recorded[14] in the case of urea, ammonium chloride, glycerin, alcohol, various glycols, antipyrine, methenamine, etc.

Most chemical substances may be classified into groups on the basis of similar osmotic properties. A study of the freezing points of different substances at the same per cent concentration fails to reveal this natural grouping, but it is apparent when concentrations are expressed in molal units. This comparison is facilitated by the use of a ratio obtained by dividing the experimentally determined freezing-point depression by the molal concentration of the solute. This ratio is referred to as the *molal lowering of the freezing point* and is defined by the equation

$$L = \Delta t / C \qquad (I)$$

L = molal lowering of the freezing point
Δt = depression of the freezing point produced by the solute (° C)
C = molal concentration of the solute

This property is fairly constant with changes in concentration and has the further advantage that salts of the same ionic type tend to exhibit the same molal lowering of the freezing point.[12] Values for the molal lowering of the freezing point, L, for many substances are tabulated in the International Critical Tables[13] and other sources. It thus becomes possible to calculate and assign an average L value for substances of a similar ionic type as shown in Table I.

In Table I a systematic use of numbers and letters has been adopted for the classification. Nonelectrolytes are 1A, weak electrolytes are 1B and simple strong electrolytes are 2, 3 or 4. The type numbers 2, 3 and 4 refer to the number of ions or particles formed by dissociation of one

TABLE I.—CLASSIFICATION OF COMPOUNDS BY IONIC TYPE WITH AVERAGE (*L*) VALUES

TYPE 1A: $L = 1.9$
Nonelectrolytes—substances which do not dissociate in solution. *Examples:* sucrose, dextrose, camphor, glycerin.

TYPE 1B: $L = 2.0$
Weak electrolytes—substances which do dissociate very slightly in solution. *Examples:* boric acid, citric acid, mercury cyanide, ephedrine base.

TYPE 2A: $L = 2.0$
Di-divalent electrolytes—substances which dissociate in solution into two ions, the anion being polyvalent. *Examples:* magnesium sulfate, cupric nitrate, zinc sulfate.

TYPE 2B: $L = 3.4$
Uni-univalent electrolytes—two ions, univalent anion. *Examples:* sodium chloride, potassium chloride, silver nitrate, ephedrine hydrochloride, pilocarpine hydrochloride.

TYPE 3A: $L = 4.3$
Uni-divalent electrolytes—three ions, polyvalent anion. *Examples:* sodium carbonate, sodium phosphate (Na_2HPO_4), atropine sulfate.

TYPE 3B: $L = 4.8$
Di-univalent electrolytes—three ions, univalent anion. *Examples:* calcium chloride, zinc chloride, magnesium chloride, zinc phenolsulfonate.

TYPE 4A: $L = 5.2$
Uni-trivalent electrolytes—four ions, trivalent anion. *Examples:* sodium citrate.

TYPE 4B: $L = 6.0$
Tri-univalent electrolytes—four ions, univalent anion. *Examples:* aluminum chloride, ferric chloride.

TYPE 5: $L = 7.6$
Tetraborates—sodium borate, potassium borate.

molecule in solution. In types 2, 3 and 4, the letter A stands for polyvalent anion, B for univalent anion.

Weak acids (all organic acids, phosphoric acid, boric acid, etc.) are not dissociated sufficiently to make a significant difference in the freezing point; thus salts of di- and tribasic acids are classified by considering the acid hydrogen as remaining attached to the negative ion. *Example:* A member of Type 2B ($NaHCO_3$, or NaH_2PO_4, or NaCl) would dissociate into two ions ($Na^+ + HCO_3^-$, or $Na^+ + H_2PO_4^-$, or $Na^+ + Cl^-$), the anion in each case being univalent.

Type 5 is an arbitrary classification reserved for tetraborates.

NOTE: This table is used only when it becomes necessary to calculate the sodium chloride equivalent for some new compound not shown in Table II.

Methods of Calculation

Many methods have been proposed for calculating the amount of salt or other substance that must be added to a hypotonic solution in order to make it isotonic with a chosen standard. The most convenient method is to calculate a sodium chloride coefficient for each substance. This coefficient is so defined that it is numerically equal to the weight of sodium chloride that would exert the same osmotic effect as would one weight unit of the substance in question. Osmotic effects of different substances in solution are thereby reduced to a common denominator, namely, the weight of sodium chloride that would exert the same osmotic effect.

The sodium chloride equivalents for a number of substances are shown in Table II and were calculated by the equation

$$E = L/M\frac{(58.45)}{(3.44)}$$

or

$$E = 17\,(L/M) \qquad \text{(II)}$$

E is the sodium chloride equivalent of a substance having molecular weight, M, and molal freezing-point depression, L. The figures 58.45 and 3.44 are the corresponding values for sodium chloride. This equation may be used to calculate the sodium chloride equivalent, E, for a substance not shown in Table II.

EXAMPLE: Calculate the NaCl equivalent (E) for potassium chloride.

KCl produces two univalent ions (like NaCl; see Table I), the anion being univalent. It is therefore type 2B, having an L value of 3.4. The molecular weight of KCl is 74.55. Substituting these values in the equation $E = 17\,(L/M)$ we have

$$E = 17\frac{(3.4)}{(74.55)} = 0.78$$

One gram of KCl is equal to 0.78 Gm. of NaCl in osmotic effect.

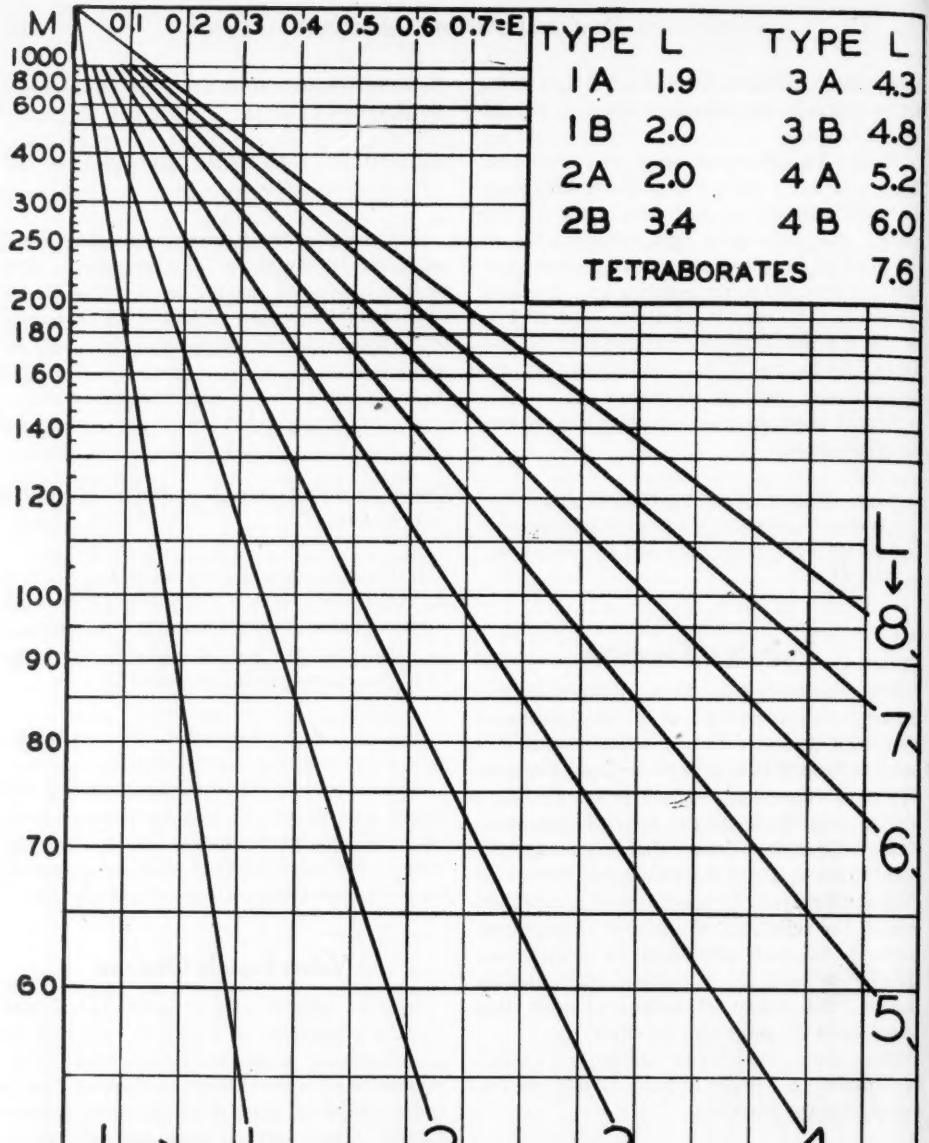
If it is more convenient in any instance to look up the freezing point of a solution of known per cent concentration, this information may be used in calculating the sodium chloride equivalent (E) by combining equations I and II:

$$E = 1.7(\Delta t/w) \qquad \text{(III)}$$

E is the sodium chloride equivalent of a substance that lowers the freezing point of water $\Delta t°$ C. at a concentration of w Gm. in 100 Gm. of water. For most practical purposes w may be the w/v per cent concentration of the substance.

Values Rapidly Obtained

Since an error of 10% or less in the E value may be permissible in practical work it is far more important to devise a rapid method for approximating sodium chloride equivalents than to spend additional time obtaining more accurate values. The chart on page 102 is a nomograph designed to solve equations II and III and is sufficiently accurate for most work. In the nomograph, molecular weights are arranged along the vertical reciprocal scale, M. Sodium chloride equivalents are arranged along the linear horizontal scale, E. For each value of the molal lowering of the freezing point, L, there is a linear relationship between the reciprocal of the molecular weights and the sodium chloride equivalent. This relationship is shown for integral values of L up to 8 by straight lines radiating from the left-hand corner of the graph.



THE NOMOGRAPH above is used for rapid calculation of sodium chloride equivalents. Determine type (Table I) and molecular weight. Select a sloping line corresponding to the L value for the type. Read the E scale where the sloping line crosses the value of the molecular weight shown on the verticle scale M. To find the sodium chloride equivalent of a compound having molecular weight of 250 and an L value of 3, locate the position of 250 on the vertical scale. Follow this line to the right until it intersects the sloping "$L = 3$" line. This point is read on the E scale as 0.2 which is the required value. When the L value includes a decimal fraction, it is usually sufficiently accurate when dealing with high molecular weights to select the sloping line corresponding to the closest integer of the actual L value. If the substance has a molecular weight below 140, it is best to interpolate for the fraction. With a little practice it is easy to interpolate for fractional values of L and to read E within one- or two-hundredths of a unit without the aid of dividers or paper scales. Although such aids will increase accuracy they are usually not needed. The Δ scale gives the approximate freezing point of a 1% solution. To find a value of E corresponding to a measured freezing-point depression in a 1% solution, locate the freezing point in ° C. on the Δ scale and read E directly above.

TABLE II.—SODIUM CHLORIDE EQUIVALENTS

Drug (salts anhydrous unless otherwise indicated)	*Type*	*NaCl Equivalent (E)*	*Drug (salts anhydrous unless otherwise indicated)*	*Type*	*NaCl Equivalent (E)*
Alypin hydrochloride (Amydricaine HCl)	2B	0.18	Phenacaine HCl.H_2O (Holocaine HCl)	2B	0.16
Ammonium chloride*	...	....	Phenol	1A	0.34
Amphetamine sulfate (Benzedrine sulf.)	3A	0.20	Physostigmine salicylate (Eserine salicyl.)	2B	0.14
Amylcaine hydrochloride	2B	0.20	Physostigmine sulfate	3A	0.12
Antipyrine*	...	....	Pilocarpine hydrochloride	2B	0.24
Apothesine hydrochloride	2B	0.19	Pilocarpine nitrate	2B	0.21
Atropine sulfate.H_2O	3A	0.11	Potassium acid phosphate (KH_2PO_4)	2B	0.40
Benzyl alcohol	1A	0.30	Potassium chloride	2B	0.78
Boric acid	1B	0.55	Procaine hydrochloride (Novocain)	2B	0.21
Butacaine sulfate (Butyn sulfate)	3A	0.10	Propadrine	2B	0.31
Calcium chloride	3B	0.73	Silver nitrate	2B	0.32
Camphor	1A	0.21	Sodium bicarbonate	2B	0.72
Chlorobutanol (Chloretone)	1A	0.18	Sodium biphos. (NaH_2PO_4)	2B	0.45
Cocaine hydrochloride	2B	0.17	Sodium biphosphate.H_2O ($NaH_2PO_4.H_2O$)	2B	0.39
Copper sulfate.$5H_2O$	2A	0.14	Sodium borate.$10H_2O$	5	0.34
Dextrose anhydrous	1A	0.18	Sodium carbonate	3A	0.68
Diothane hydrochloride	2B	0.13	Sodium chloride	2B	1.00
Emetine hydrochloride	3B	0.15	Sodium citrate.$2H_2O$	4A	0.30
Ephedrine hydrochloride	2B	0.29	Sodium hypophosphite.H_2O	2B	0.54
Ephedrine sulfate	3A	0.17	Sodium iodide	2B	0.38
Epinephrine hydrochloride	2B	0.26	Sodium lactate	2B	0.52
Ethylmorphine HCl.$2H_2O$ (Dionin)	2B	0.15	Sodium nitrate	2B	0.68
Ethylhydrocuprein hydrochloride (Optochin)	2B	0.15	Sodium phosphate.$2H_2O$ ($Na_2HPO_4.2H_2O$)	3A	0.41
Eucatropine hydrochloride (Euphthalmine)	2B	0.18	Sodium phosphate.$7H_2O$	3A	0.27
Fluorescein soluble	3A	0.19	Sodium phosphate.$12H_2O$	3A	0.20
Glycerin*	...	....	Sodium sulfite	3A	0.58
Homatropine hydrobromide	2B	0.16	Sucrose	1A	0.10
Hyoscine HBr.$3H_2O$ (Scopolamine HBr)	2B	0.13	Sulfadiazine sodium	2B	0.21
Hyoscine hydrochloride.$2H_2O$	2B	0.15	Sulfanilamide	1B	0.20
Lactose.H_2O	1A	0.09	Sulfapyridine sodium.H_2O	2B	0.20
Larocaine hydrochloride	2B	0.18	Sulfathiazole sodium sesquihydrate	2B	0.19
Magnesium chloride	3B	0.86	Syntropan	2B	0.14
Menthol	1A	0.21	Tannic acid	1B	0.10
Mercuric chloride	1B	0.13	Tetracaine hydrochloride (Pontocaine HCl)	2B	0.19
Mercuric cyanide	1B	0.14	Tutocain hydrochloride (Butamin)	2B	0.20
Methenamine*	...	....	Urea*	...	....
Metycaine hydrochloride	2B	0.20	Zinc chloride	3B	0.60
Morphine hydrochloride.$3H_2O$	2B	0.15	Zinc phenolsulfonate.$8H_2O$	3B	0.15
Morphine sulfate.$5H_2O$	3A	0.10	Zinc sulfate.$7H_2O$	2A	0.12
Neo-synephrin hydrochloride	2B	0.28			
Nupercaine hydrochloride	2B	0.15			

NOTE: The values for *E* may be used as either grams or grains depending upon which system of weights the prescription specifies.

* These substances have been recorded as being exceptions to the general rule (see discussion) and may be disregarded when calculating isotonicity.

Application to Prescriptions

To prepare an isotonic solution on prescription, the weight of each substance present in a definite volume is multiplied by the respective E value. The sum of these products is subtracted from the weight of sodium chloride required to make the original volume of distilled water isotonic. The result of this subtraction is the amount of sodium chloride that must be added to render the solution isotonic.

AMOUNT NaCl NEEDED FOR ISOTONICITY WITH BLOOD SERUM AND TISSUE FLUIDS IN GENERAL

0.9 Gm. of NaCl per 100 cc.
0.27 Gm. of NaCl per 30 c.c.
4.1 grains of NaCl per fluid ounce

NaCl NEEDED FOR ISOTONICITY WITH TEARS

1.4 Gm. of NaCl per 100 cc.
0.42 Gm. of NaCl per 30 cc.
6.37 grains of NaCl per fluid ounce

NOTE: While it may be customary to make collyria isotonic with tears, there seems to be no very good reason for continuing this practice. There is good evidence that solutions isotonic with blood serum are entirely satisfactory for use in the eye.[12]

Examples of Calculations

1. *How much sodium chloride must be added to 100 cc. of a 2% solution of procaine hydrochloride to render it isotonic for injection?*

100 cc. of isotonic solution contains	0.90 Gm. NaCl
Procaine hydrochloride, $E = 0.21$ (see Table II) 2 Gm. $\times$ 0.21 =	0.42 Gm. NaCl
To render solution isotonic add	0.48 Gm. NaCl

Should it be necessary to render the solution isotonic by the addition of any other substance, first determine the weight of sodium chloride which should be added (as above), then divide this weight by the E value for the substance used to replace sodium chloride. The result of this division gives the required weight of the other substance.

2. ℞

Zinc sulfate	gr. i
Boric acid	gr. x
Aqua dest., q. s.	℥ i

M. Ft. Isotonic c̄ NaCl
Sig: Eye drops

℥i of isotonic solution contains	6.37 grains NaCl
Zinc sulfate, $E = 0.12$; then $1 \times 0.12 = 0.12$	grains NaCl
Boric acid, $E = 0.55$; then $10 \times 0.55 = 5.50$	grains NaCl
Total equivalent represented by drugs $(0.12 + 5.50) =$	5.62 grains NaCl
To render solution isotonic add	0.75 grains NaCl

3. ℞

Ephedrine sulfate	0.60
Chlorobutanol	0.12
Aqua dest., q. s.	30.0

M. Ft. Isotonic
Sig.: Nose drops

30 cc. of isotonic solution contains	0.27 Gm. NaCl
Ephedrine sulfate, $0.60 \times (E)$ $0.17 = 0.10$	Gm. NaCl
Chlorobutanol, $0.12 \times (E)$ $0.18 = 0.02$	Gm. NaCl
Total equivalent represented by drugs $(0.10 + 0.02) =$	0.12 Gm. NaCl
To render solution isotonic add	0.15 Gm. NaCl

Adjusting Buffered Solution

A hypotonic buffered solution may be rendered isotonic simply by considering the sodium chloride equivalent as represented by the amount of buffer salts present. The sodium chloride equivalents (E) shown at right for Gifford's buffer solutions and Sörensen's phosphate buffer are calculated in terms of *grams* per specified volume; whereas the sodium chloride equivalents (E) in Table II were calculated as units and can be called either grams or grains.

4. ℞

Pilocarpine hydrochloride..... 0.3
Buffer pH 6.8 (Sörensen), q. s...... 30.0

M. Ft. Isotonic c̄ tears
Sig: Use as directed in both eyes

30 cc. of isotonic solution contains..... 0.42 Gm. NaCl
Pilocarpine hydrochloride, 0.3 × (*E*) 0.24 = 0.07 Gm. NaCl
30 cc. Sörensen Buffer, *p*H 6.8, (*E*, see Table *IV*) = 0.13 Gm. NaCl
Total equivalent represented by drug and buffer..... 0.20 Gm. NaCl
To render solution isotonic add 0.22 Gm. NaCl

If the above prescription were made isotonic with blood serum instead of tears, 0.07 Gm. sodium chloride would be added:

30 cc. of isotonic solution contains..... 0.27 Gm. NaCl
Total equivalent represented by drug and buffer..... 0.20 Gm. NaCl
To render solution isotonic add 0.07 Gm. NaCl

Summary

Substances of the same ionic type have nearly the same molal freezing-point depression. This fact is used as the basis for estimating approximate isotonic concentrations of substances for which freezing-point data are lacking. Equations are shown that are used where either approximations or exact cryoscopic data are employed. These equations are used to compute the weight of sodium chloride that would have the same osmotic effect as one unit weight of the substance under consideration. A graphic method is provided for rapid calculation of the sodium chloride equivalent, either from ionic type and molecular weight, or from the freezing point of 1% solutions. Tables of sodium chloride equivalents are given for 80 substances and for two sets of buffers. Examples are shown illus-

TABLE III.—GIFFORD BUFFER SOLUTIONS

STOCK SODIUM CARBONATE SOLUTION

Sodium carbonate, anhydrous	21.2 Gm.
Distilled water, recently boiled, *q. s.*.....	1000.0 cc.

1 cc. = 0.014 Gm. (E) sodium chloride

STOCK ACID BUFFER SOLUTION NO. 1

Boric acid crystals, anhydrous	12.4 Gm.
Potassium chloride, anhydrous.....	7.4 Gm.
Distilled water, recently boiled, *q. s.*.....	1000.0 cc.

1 cc. = 0.013 Gm. (E) sodium chloride
30 cc. = 0.380 Gm. (E) sodium chloride

TABLE IV.—SÖRENSEN'S BUFFERS FOR THE pH RANGE 5.91 TO 8.04

0.0667 Molar NaH_2PO_4, cc.		*0.0667 Molar Na_2HPO_4, cc.*	*p*H	*100 cc. of Buffer Equivalent to (E) GRAMS NaCl*	*30 cc. of Buffer Equivalent to (E) GRAMS NaCl*
9	+	1	5.91	0.38	0.114
8	+	2	6.24	0.39	0.117
7	+	3	6.47	0.40	0.120
6	+	4	6.64	0.41	0.123
5	+	5	6.81	0.42	0.126
4	+	6	6.98	0.44	0.132
3	+	7	7.17	0.45	0.135
2	+	8	7.38	0.46	0.138
1	+	9	7.73	0.47	0.141
0.5	+	9.5	8.04	0.48	0.144

NOTE: The 0.0667 molar concentrations, as given, are for the anhydrous salts. If a hydrated salt is used, the water of crystallization must be taken into consideration in the molecular weight.

trating the ease of calculating isotonic solutions when the sodium chloride equivalent for a substance is known. Certain substances reversibly permeate cellular tissue with sufficient rapidity that little or no osmotic effect is exerted. A few of these substances have been indicated and may be disregarded when calculating the isotonicity of such solutions. Further investigative work is being done on these special substances.

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U. S. P. DEVELOPS PENICILLIN MONOGRAPH

PENICILLIN may soon be available for civilian use, according to information received by the U. S. P. Committee on Revision, and steps are being taken to speed development of Pharmacopœial standards.

White, crystalline penicillin sodium has been isolated by three manufacturing laboratories, and this material will probably be made the official reference standard when an ample quantity with proved stability, say 60 Gm., is available. The pure salt is believed to have a potency of about 1650 Oxford units per milligram.

Potency of 1 mg. of reference standard will be checked in terms of the biologically measured Oxford unit, according to present plans, so that a standard of comparison will be available when referring to the Oxford dosages given in the older medical literature. All statements of potency for official preparations, however, will be expressed in milligrams of the reference standard, according to the tentative monograph. Thus physicians will soon become familiar with the simpler metric dosage and probably use it exclusively.

It is hoped that the same lot of the drug used for the U. S. P. reference standard will be accepted by Great Britain and Canada as their reference standard and that the League of Nations Committee will adopt it as the International Reference Standard.

Penicillin sodium is the proposed official title. When a calcium compound of penicillin or other preparation becomes available, it is planned that it will be similarly standardized under an appropriate title.

Penicillin sodium is described in the tentative monograph as occurring "as a fine powder or as granules or scales, and may be white or naturally colored." Pharmacists will have to store the drug at a temperature not above 10° C. as it is usually adversely affected by moisture and elevated temperatures.

The warning about storage temperature must appear on the label, together with the lot number, date beyond which potency is not guaranteed, and a statement of the bacteriostatic activity of the contents of the container in terms of milligrams of U. S. P. reference standard.

Facilities for producing penicillin in the United States are being increased rapidly, and by July it is expected that 21 laboratories will be operating at full capacity. An estimated 21,092,000,000 Oxford units, or the equivalent of 12,783 Gm. of penicillin sodium, were produced in 1943, according to WPB's Chemical Bureau. Between 200,000 and 1,000,000 Oxford units are usually used per case. The cost of the drug would thus be between $6.50 and $32.50 per patient at present. The cost is expected to go much lower as the production rate is multiplied manyfold.

Drugs Used for
ALLEVIATING SPRING INFLAMMATIONS

by MELVIN W. GREEN

CHAIRMAN, COMMITTEE ON PHARMACEUTICAL RECIPE BOOK

PROTECTIVES, ASTRINGENTS AND COUNTERIRRITANTS ARE DISCUSSED HERE IN ANOTHER TIMELY ARTICLE OF A SERIES

HOUSEHOLDS again buzz with springtime activities, and the lawn mower, rug beater and victory garden implements are wielded with the usual early season vigor. A by-product of these endeavors is an increased demand for household liniments, astringents, dusting powders and similar preparations to alleviate bruises, sprains and other types of inflammation. The pharmacist should be well informed concerning the nature of the inflammatory process and methods for its alleviation so that he can cooperate with the physician to the greatest possible extent concerning drugs used for this purpose. Let us take some seasonal pharmaceutical exercise by reviewing the nature and uses of these drugs, which include the protectives, such as emollients, demulcents, dusting powders; the irritants, particularly those used for producing counterirritation; and the astringents.

Before discussing the drugs, a brief word should be said concerning the nature of the inflammatory process. An inflamed tissue is characterized by redness, swelling, an increased local temperature and pain. Most of these phenomena can be traced to the local dilation of the blood vessels in the inflamed areas. Because the blood vessels are dilated and perhaps due to the liberation of definite chemical substances in the neighborhood of the injury, the permeability of the capillaries is changed, permitting the plasma to exude into the tissue spaces, thus giving rise to swelling. This swelling produces a pressure on the sensory nerve endings which is responsible for the pain. The temperature rise in the inflamed area is also due to the vasodilation which causes more blood to be brought to the surface. The redness is caused by the same condition.

Drugs that increase inflammation are known as phlogominetic drugs; those drugs which alleviate or prevent inflammation are known as antiphlogistic drugs. Antiseptics should really fall in this last category since, by killing or inhibiting bacteria, they alleviate or, better still, prevent inflammation. However, these drugs will not be discussed at this time.

Protectives

Protectives act in a more or less mechanical fashion to protect raw, inflamed tissues from the action of the air and other sources of irritation. Dusting powders, mechanical protectives, emollients and demulcents belong in this group. Any finely divided dry powder that is insoluble in tissue fluids may serve as a dusting powder to provide mechanical protection. Powders having a flake-like crystal structure, such as zinc stearate, are particularly advantageous. In addition, powders soak up fluids in the affected area, thus serving to impede bacterial invasion. Purified talc, kaolin, iodoform thymol iodide, boric acid, zinc stearate, zinc oxide and many other substances are useful for this purpose.

The *Pharmaceutical Recipe Book* contains several formulas for useful combinations of these drugs. Some of these powders contain antiseptics, such as boric acid or calomel, and astringents, particularly alum. Compound Ammoniated Mercury Dusting Powder with Zinc Oxide, Boric Acid and Zinc Carbonate; Borated Dusting Powder; Boric Acid, Bismuth and Calomel Dusting Powder; Boric Acid and Starch Dusting Powder; Zinc and Boric Acid Dusting Powder; Salicylic and Benzoic Acid Dusting Powder and others are listed in the *Pharmaceutical Recipe Book*. The original formulas for these compounds in many instances were taken from hospital formularies and foreign compendia.

The mechanical protectives include such things as Flexible Collodion and resins. The Chloroformic Solution of Tar of the National Formulary is very useful for this purpose since

the chloroform, upon evaporation, leaves a thin film of resin which protects the injured area. As the chloroform evaporates there may be a temporary irritation, particularly around hairy surfaces, but this soon subsides when evaporation is complete.

The demulcents are usually colloidal substances, such as gums, starches or oils, used to protect mucous membranes against mechanical injury. Lubricants for instrumentations, such as catheter lubricants, belong to this class, and formulas for several such preparations are to be found in the *Pharmaceutical Recipe Book*. The emollients on the other hand, are usually fatty substances used to protect abraded skin against mechanical injury.

Irritants and Counterirritation

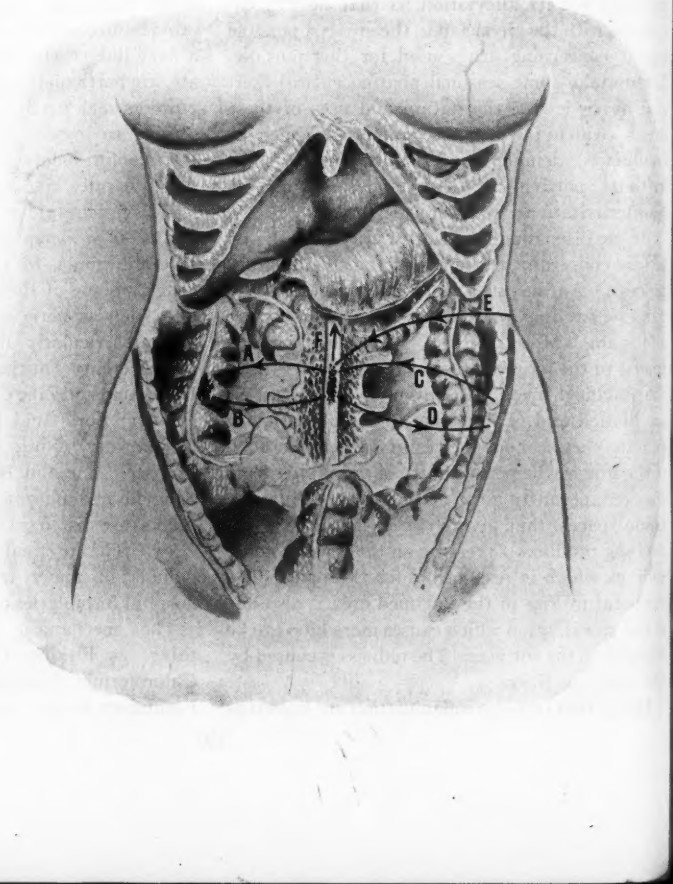
Many drugs and foreign bodies produce local irritation on the skin and mucous membranes. This irritation is brought about by withdrawing fluid from the cells, precipitating the proteins of the cells, dissolving the cell or some part of the cell, and by some other processes, the nature of which is not well known.

These irritants set up an inflammatory process at their point of contact. Although usually we wish to avoid irritant action, the properties of irritants are frequently employed to produce a desirable therapeutic effect.

Carminatives, locally acting emetics, and purgatives are irritant drugs acting upon the mucous membrane of the gastrointestinal tract. For the present, however, our discussion will be confined to those drugs which are used for their local irritant action on the skin and mucous membrane, primarily to alter normal local circulation and nutrition of the affected part. Obviously these drugs are used to bring about a better circulation and nutrition to muscular tissue when it is strained or bruised. The use of most liniments is based on this action. That is, the irritation produces local vasodilation which brings about increased nourishment of the tissues and local heat.

In addition to inflammation in the skin and musculature caused by local injury due to bruising and straining, inflammation often occurs as a result of some disease or injury to the more remote viscera. This is brought about by "referred pain," the physiology of which is very interesting, although still somewhat speculative.

The visceral organs, such as the intestines, stomach and heart are considered to be incapable of recognizing pain directly. It is a well-known fact that the surgeon may handle the intestine without causing appreciable pain to the patient. On the other hand, it is equally well known that when the intestine is inflamed due to the presence of some strong irritant or pathological condition, such as an infected appendix or an ulcer, some



particular area of abdominal muscle and skin becomes inflamed, tender to the touch, and very rigid. The pain is thus "felt" in this remote area rather than in the diseased organ itself. Something of the same phenomenon is experienced in spasms of the coronary artery in the heart. The pain is often expressed as "shooting down the left arm."

The anatomical drawing on page 108 illustrates the mechanism by which this pain, arising in the viscera, is referred to a more superficial region. Let us assume that the intestine is diseased. Impulses from this injured area are carried more rapidly than normally across nerve *B*, as shown in the drawing, to the juncture of the nerve with the spinal cord. Nerve *A* carries impulses from the cord to the intestine. Because these impulses are arising at an abnormal rate in the cord, an area of hyperexcitability is set up in the region of the cord indicated on the drawing by the stippled area. Normally, impulses go out from this area of the cord to muscles in that approximate vicinity at a relatively slow rate. However, since the area of the cord is now in a very excited state, a much greater number of impulses go over nerve *D* and the muscle feels much more rigid to the touch than would be expected. Thus, the muscles and skin in this remote area are inflamed by the process of referred pain, the pain being referred from the injured intestine.

If mild irritants are applied to the area involved, they frequently aid in alleviating this pain. The mode of action of these irritants, which are said to be producing counterirritation, is not completely clear. It is supposed that the impulses now going over nerve *E* from the skin and nerve *C* from the muscles will somehow block the impulses from the hyperexcited area and prevent them from going across the nerve channels of the cord *F* to the higher interpretive centers of the brain. Mustard plasters and various other irritant drugs are used to produce this counterirritant action.

Irritants are commonly classified, according to the severity of the inflammation which they produce, as rubefacients, vesicants and pustulants. Rubefacients are those drugs which produce no greater inflammation than is characterized by redness of the part to which the irritant is applied. Irritants acting so severely that they cause the serum and white blood cells to leave the blood vessels and go out into the tissue spaces, thus producing a blister, are known as vesicants. Irritants acting still more severely and causing the appearance of little blisters containing sterile pus are known as pustulants. Although at one time it was quite fashionable for physicians to use drugs for their pustulant and vesicant effects, this is done very infrequently at present. Drugs that are used as counterirritants are now usually selected by the physician because they are capable of producing a rubefacient action only.

Some drugs used as irritants are so mild in their action that there is never more than a therapeutic degree of irritation. But many drugs in this category may produce a corrosive action on the tissues if the concentration is high or if they are left in contact with the tissues too long. Persons inadvisedly attempting self-medication with irritants should therefore be warned of the possible dangers involved, and the danger of applying a bandage over Tincture of Iodine should be pointed out especially.

Iodine Useful

The pharmacist should recall that the official Tincture of Iodine (7%) is useful as a counterirritant but it is much too caustic as an antiseptic. The official Liquor Iodi or Tinctura Iodi Mitis are preferable as antiseptics. First aid courses are stressing to the laity the use of the mild tincture and the pharmacist should keep his patrons informed of the fact.

Liniments containing mildly irritating drugs are frequently used for producing counterirritation. Although the official compendia contain a number of preparations for this purpose, such as Chloroform Liniment, the physician may desire to prescribe a somewhat different formula. The new *Pharmaceutical Recipe Book* contains the formulas for a number of these preparations, such as Ammonia and Camphor Liniment, Compound Capsicum Liniment, Balsamic Capsicum Liniment, Menthol Liniment, Compound Methyl Salicylate Liniment, Compound Liniment of Mustard and many others.

Older physicians, particularly, sometimes resort to the use of poultices for alleviating inflamed areas. The *Pharmaceutical Recipe Book* contains formulas for poultices such as Slippery Elm Poultice, Mustard Poultice, Phenol and Linseed Poultice and Boric Acid Poultice. Cataplasm of Kaolin, N. F., and Bread or Linseed Poultices are frequently employed as household remedies. Directions for preparing the latter

two may be found in the *Pharmaceutical Recipe Book*.

With the advent of heating devices capable of producing and holding a high temperature for long periods, heat methods are rapidly replacing drugs for counterirritant purposes. Electric heating pads, infrared heat lamps and similar devices show much promise in this field and may some day supplant many of the older remedies. Since the pharmacist frequently distributes these devices, it is advisable that he know as much about their effectiveness and limitations as he can.

Astringents

Astringents, when applied to an inflamed mucous membrane or a wound, produce a thin protective film on the surface, diminish secretions, check the migration of leucocytes and formation of pus, and contract superficial and deeper tissues. Agents that have a strong precipitant action on proteins can go beyond mere astringency and produce irritation or kill the tissues. Consequently most astringents should be applied only with care and medical supervision. The concentration, the solubility and the time of contact determine whether a given substance will act as an astringent, an irritant or a caustic.

The drugs most frequently prescribed for their astringent effects are tannic acid and drugs containing tannin, dilute solutions of salts of metals other than the alkali metals, certain dilute organic acids, dilute alcohol and glycerin. Alcohol and glycerin alone are relatively ineffective but when used in conjunction with other astringents are frequently of value. Alum, solution of iron chloride and Monsell's Solution aree ffective but very drastic astringents. It is worth noting that tannic acid has been demonstrated to be toxic to the liver when used as an astringent over wide areas, as in burns.

Astringents are of use to physicians for the protection of inflamed and wounded mucous surfaces and to contract swollen and chronically inflamed areas. They also help to reduce the secretions of certain types of wounds. Astringents are often used for their local styptic action, since by protein precipitation they frequently stop capillary oozing. Internally, they are sometimes employed to diminish diarrhea.

Probably the most frequently prescribed external astringent is Burrow's Solution, for it seems to be less irritant to abraded surfaces than solution of alum. A European remedy, official in the French Codex, is Alibour Water. The formula appears in the *Pharmaceutical Recipe Book* and a discussion of its preparation and use has been published in THIS JOURNAL (3: 378, 1942, Nov.). The *Recipe Book* also contains the formulas for a number of astringent solutions to be applied externally, such as Ulzman's Solution, Compound Solution of Zinc and Aluminum, Solution of Aluminum Aceticotartrate, Solution of Aluminum Citrate (a discussion of solutions of aluminum citrate is found in THIS JOURNAL, 3: 134, 1942, April), Lead and Zinc Lotion, Astringent Lotion, and Compound Infusion of Rose. In addition, formulas are given for a number of douche powders, astringent dusting powders and astringent ointments. Many of the species found in the *Pharmaceutical Recipe Book*, particularly those used in baths, are mildly astringent.

One of the most frequent uses of astringents is to relieve congested hemorrhoids. Most physicians have a particular formula they like to use for this purpose but since the patient is frequently a chronic sufferer, the physician often desires to make an occasional change. A number of formulas for astringent suppositories are available in the *Pharmaceutical Recipe Book* which will usually fill the physician's needs.

Astringents are used internally, particularly to alleviate diarrhea. The astringent drugs are not used for this purpose as much as formerly, but older physicians may still care to use them. Many formulas are in the *Pharmaceutical Recipe Book* for this purpose, such as Mixture of Bismuth and Camphorated Opium; Compound Mixture of Opium and Chalk; Aromatic Chalk Mixture; Mixture of Opium, Rhubarb and Gambir; Tincture of Krameria; Syrup of Blackberry Bark; and Sweet Tablets of Albumin Tannate. It must be remembered that preparations containing opium act by diminishing the activity of the intestinal tract rather than by simple astringent action.

Drugs to stop diarrhea should never be dispensed without a physician's order, for the presence of diarrhea is frequently a sign of some more serious poisoning or disease of the gastrointestinal tract.

More Active
OINTMENT OF MERCUROUS IODIDE

by PAUL V. MANEY and RUDOLPH A. KUEVER
COLLEGE OF PHARMACY, STATE UNIVERSITY OF IOWA

NEW SUSPENSION IN SPECIAL HYDROPHILIC BASE PROVIDES HIGH BACTERIOSTATIC ACTION

OINTMENTS of mercury salts have received considerable attention in recent years. Definite progress is being made in developing more useful preparations with greater bacteriostatic properties. Vicher, Snyder and Gathercoal,[1] using a method developed by Broady and Jordan,[2] prepared what they termed "colloidal calomel" from which they compounded calomel ointments of various strengths. The ointments prepared in this manner exhibited greater antiseptic values than the official Ointment of Mild Mercurous Chloride. More recently, Kuever and Burnside[3] developed a stable form of ointment of mercuric nitrate, which, with the same mercuric nitrate content, is more than three times as potent as Ointment of Mercuric Nitrate, N. F.

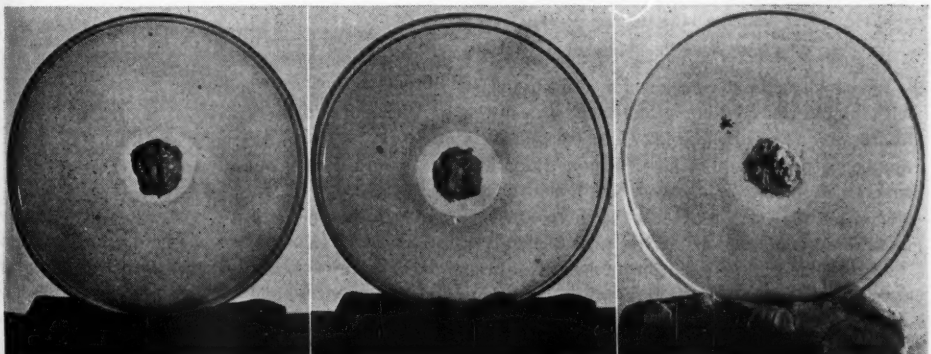
Moreover there are new ointment bases of the hydrophile type which lend themselves well to obtaining maximum therapeutic activity of the bacteriostatic ingredients.[4]

Having this progress in mind, and the fact that mercurous iodide has displayed useful and potent properties, the problem of preparing it in finely divided form for purposes of making ointments presented itself.

The preparation of a stable mercurous iodide suspension consists of adding a cold dilute solution of potassium iodide and a protective colloid to a cold dilute solution of mercurous nitrate with constant stirring. Gelatin and acacia are generally employed as protective colloids; however, in view of the precipitating action of certain mercury salts upon gelatin, acacia and similar substances, an inert colloid was selected. Investigation disclosed that methyl cellulose could be employed and that it possessed many desirable properties.

The following general method was developed:

Dissolve 20 Gm. of methyl cellulose and 44 Gm. of potassium iodide in 2500 cc. of cold dis-



BACTERIOSTATIC ACTION of finely precipitated mercurous iodide in 1% ointments is demonstrated by the agar plates shown above after 48 hours incubation at 37° C. Staphylococcus aureus from a 24-hour broth culture was used as the test organism. The new form of mercurous iodide incorporated in U. S. P. White Ointment base (left) has produced a 3–4 mm. zone of inhibition; the mercurous iodide in the newly developed hydrophilic base (center) produced a 6–7 mm. zone; when this same ointment is adjusted to pH 4.5 with lactic acid (right), the zone of inhibition has a diameter of 8–10 mm.

tilled water. Dissolve 75 Gm. of mercurous nitrate in 2500 cc. of distilled water containing one per cent of nitric acid. Add the potassium iodide-methyl cellulose solution drop by drop (at the rate of one drop per second) to the mercurous nitrate solution with constant stirring. Wash the suspension by dialysis until it is free from acidity and soluble salts. Concentrate by evaporation in vacuum, or by centrifuging. Assay according to the method of the National Formulary.[5] Test for the presence of mercuric chloride and other undesirable contamination by N. F. procedures.[5]

The mercurous iodide suspension prepared in the above manner cannot be considered as colloidal, any more than the Broady and Jordan method will yield a colloidal calomel, but it does represent a very fine state of division.

In the process described, it is important that the solution of potassium iodide be added to the solution of mercurous nitrate. This order of mixing prevents the formation of metallic mercury and mercuric iodide.[6] If the order of mixing is reversed, the mercuric iodide formed reacts with the excess potassium iodide to form potassium mercuric iodide, which is soluble.

When the potassium iodide solution is poured into the mercurous nitrate solution by the correct procedure, the reaction is as follows:

$$KI + HgNO_3 \rightarrow HgI + KNO_3$$

If the mercuric nitrate solution is poured into the potassium iodide solution, the reactions may be expressed:

$$2HgNO_3 + 2KI \rightarrow HgI_2 + Hg + 2KNO_3$$
$$HgI_2 + 2KI \rightarrow HgK_2I_4$$

Inasmuch as the suspension of mercurous iodide has a high water content, an ointment base of the hydrophilic type is required. Experiments by a number of investigators have demonstrated the superior properties of a base of this type over the official petrolatum base.[4] Furthermore, there is more rapid penetration of active ingredients.

After some experimentation, a base has been developed which is compatible with mercurous iodide, and which, when mixed with an equal weight of the mercurous iodide suspension, produces an ointment of satisfactory consistency.

This hydrophilic base is readily capable of absorbing an equal weight of water to make a completely satisfactory ointment. Highly concentrating the mercurous iodide suspension is therefore unnecessary, and the risk of destroying its desirable properties by undue exposure is eliminated.

The formula for the proposed ointment of mercurous iodide, 1%, is as follows:

Cetyl alcohol	11.5%
White petrolatum	30. %
Lanolin	8.5%
Mercurous iodide suspension (2%).	50. %

The cetyl alcohol, white petrolatum and lanolin are melted together on a water bath, and the mercurous iodide suspension, warmed to 50° C., is added slowly to the melted base with constant stirring or trituration.

The ointment is prepared without contact of metals or undue exposure to light.

To ascertain the bacteriostatic value of the proposed ointment, the F. D. A. Agar Plate Method was employed.[7] The test organism was *Staphylococcus aureus*.

A series of 1% mercurous iodide ointments was prepared and tested. The diffusion and bacteriostatic potency are tabulated below:

Ointment	*Diffusion**	*Inhibition Zone*
N. F. Mercurous Iodide 1% in U. S. P. White Ointment	Poor	None
N. F. Mercurous Iodide 1% in Proposed Hydrophilic Base	Good	None
Proposed Suspended Mercurous Iodide in U. S. P. White Ointment	Slight	3–4 mm.
Proposed Suspended Mercurous Iodide in Proposed Hydrophilic Base	Good	6–7 mm.

* The term diffusion designates the actual penetration of the culture medium by the ointment.[7]

It is well known that ointments that are acidic have greater bacteriostatic potency.[8] Harrow and Sherwin[9] have pointed out that "eccrine sweat" has a *p*H 4.5, the acidity being due to the presence of lactic acid.

When the proposed ointment of mercurous iodide is made acidic by adjusting the methyl cellulose suspension to a *p*H of 4.5 by means of lactic acid, the bacteriostatic potency is appreciably increased, as the zone of inhibition clearly demonstrates (see page 111).

Summary

1. A new mercurous iodide suspension has been prepared by means of a new synthetic colloid, which can be readily incorporated directly into a hydrophilic ointment base.

2. A new hydrophilic ointment base has been developed which permits high bacteriostatic activity of mercurous iodide under proper conditions.

3. An ointment of N. F. mercurous iodide in a U. S. P. White Ointment exhibits no bacteriostatic properties.

4. An ointment of the proposed suspended mercurous iodide prepared with the proposed hydrophilic base has an appreciably greater bacteriostatic potency than an ointment made with the proposed suspended mercurous iodide using U. S. P. White Ointment as the base.

5. Stored in opal jars, at room temperature, the proposed ointment shows no signs of deterioration after four months.

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Rx PRESCRIPTION *Information* SERVICE

PROFESSIONAL PROBLEMS OF PHARMACISTS ANSWERED. BOARD OF 11 PHARMACEUTICAL SPECIALISTS AND A. PH. A. LIBRARY AND LABORATORY FACILITIES AVAILABLE TO OUR READERS. SEND QUERIES DIRECTLY TO PRACTICAL PHARMACY EDITION GIVING ALL PERTINENT INFORMATION

JAPANESE SOLDIERS CARRY WHITE, CRYSTALLINE DRUG

On some of the Japanese soldiers we have found a white crystalline powder apparently labeled Fukune Anchinepurinsan. Could you give us some clue to the identity of the drug?—J. L., South Pacific.

Two authorities agree that the drug is an antipyretic, probably a derivative of acetanilid, although it is impossible to be certain without seeing the original Japanese script. The *Fukune* could mean "bi-radical" or "a double salt," or it could mean "bivalent." There is also the possibility that Fukune is an incorrect rendering of Japanese characters which should be transliterated Fukube. This latter term is used by Japanese pharmacists, it is believed, to indicate compound powders.

One authority holds that the term *Anchinepurinsan* has definitely been transliterated incorrectly. The Japanese characters corresponding to *he* could easily be mistaken for *ne*, and *bu* characters misread as *pu*. Based on this assumption, Fukune Anchiheburinsan would mean a derivative of antifebrin, a synonym for acetanilid.

A second authority concurs in the opinion that *Fukune* probably means "double salt," that *Anchi* means "anti," and that *nepu* roughly translates to "fever." He further ventures the opinion that *rinsan* may indicate a phosphate salt.

SHAMPOO BECOMES CLOUDY

We have been preparing a neutral soapless shampoo of the following formula:

Aerosol (O. T. 100%)	*40*
Ethyl alcohol	*50*
Mineral oil	*2.15*
Lecithin	*1.87*
Cetyl alcohol	*12.5*
Aqua, q. s. ad	*250*

Up to about 12 hours after compounding the preparation is perfectly clear, as desired. Then it becomes very cloudy—almost milky. Will you please advise us how to obtain a clear product?—J. Z., N. Y.

The difficulty seems to be one of temperature control. When prepared in the laboratory of one of our consultants, the shampoo remained perfectly clear during the day but showed cloudiness as the temperature went down at night. At really cold temperatures the preparation actually assumed the appearance of a jell. The basic difficulty probably lies in the quantity of cetyl alcohol used. A few experiments reducing this quantity might produce satisfactory results. The basic formula of the shampoo was originated by the American Cyanamid & Chemical Corporation, makers of aerosol, and they indicate that they were not entirely satisfied with the formulas which were originally proposed and have abandoned further efforts to produce soapless shampoos of this type.

Would it not be satisfactory to indicate on the label that a slight warming of the shampoo might be necessary should it become chilled?

COLOR OF POWDER VARIES

For a decade we have been making the following hygienic douche powder for a local physician, but have always experienced great difficulty in obtaining a uniform product.

Boric acid, powder	*2 lb.*
Potassium alum, powder	*8 oz.*
Liquefied phenol	*3 oz.*
Oil of peppermint	*1½ oz.*

Using identical chemicals made by the same laboratory, using all glass or horn apparatus, always mixing the ingredients in the same order, and storing in tightly covered glass jars, the finished product is invariably a different color. This change of color is pronounced and occurs in strong shades of various colors. The medicinal action is apparently unchanged. Can you determine the cause of the color change and recommend remedial measures? Would you also advise whether there is a chemical which can be substituted for the scarce oil of peppermint used in the above formula?—E. L., N. Y.

The color reactions are undoubtedly caused by oxidation of the phenol. Although the method of preparation has been standardized, there is probably some slight difference either in the ingredients or the procedure. Alum is very apt to contain traces of iron and, although the U. S. P. gives a limit for these impurities, it is quite possible that the amount varies in different lots of alum. This also applies to heavy metals in both the alum and boric acid. Phenol will react with these various substances to give oxidation products which would show the color reactions indicated.

Avoid Moisture

It is likely that these reactions are facilitated by moisture from the water of crystallization in the alum. More uniform results quite probably would be obtained if exsiccated alum were to replace the official alum that contains 12 molecules of water. This, of course, should be used in proportionate quantity to represent the alum in the original formula.

Phenol will also react with oil of peppermint, and it is suggested that the liquefied phenol be mixed with part of the powders, and the oil of peppermint be mixed with another portion of the powders, finally mixing these two portions together. Thus the phenol and oil of peppermint will be kept separated as far as possible.

Menthol might be used in the formula, but wartime conditions make menthol just as critical as oil of peppermint itself. There are, however, certain synthetic menthols available which the physician might be willing to use. They are not yet official but it is likely that they will be recognized in the near future. Meanwhile, one of the synthetic products should prove satisfactory in a preparation of this type. Experiments would have to be made to determine the replacement

value. Oil of peppermint contains about 50% of total menthols. Although this figure gives some indication of the amount which might be required, less menthol than the theoretical amount will probably be needed.

A formula appearing on page 18 of Pharmaceutical Recipe Book III is basically like the one discussed. This formula originated at the Presbyterian Hospital, New York City.

WANTS VETERINARY LINIMENT

It will be very much appreciated if you will supply us with a formula or formulas for a strong veterinary liniment. Can you also suggest a good book of veterinary formulas?—I. S., N. Y.

Two widely used formulas for veterinary liniments are given in Pharmaceutical Recipe Book III. A liniment often prescribed for cattle may be prepared as follows:

Strong Solution of Ammonia	15 cc.
Oleic acid	30 cc.
Ammonium chloride	4 Gm.
Methyl salicylate	30 cc.
Oil of turpentine	90 cc.
Water, *q. s. ad*	1000 cc.

Place the Strong Solution of Ammonia in a liter bottle, add 125 cc. of lukewarm water, mix, add the oleic acid and shake well. Then add the ammonium chloride dissolved in 125 cc. of water. Stir in the methyl salicylate and another 125-cc. portion of water and shake again. Add the oil of turpentine, make up to 1000 cc. with warm water and mix and shake well. Set the liniment aside for a week.

A strong liniment listed under the R. B. III preparations for horses contains:

Tincture of Capsicum	16 cc.
Tincture of Cantharides	16 cc.
Camphor and Soap Liniment	125 cc.
Alcohol	250 cc.
Water, *q. s. ad*	1000 cc.

Mix the tinctures with the alcohol. Add this to the Camphor and Soap Liniment and water, which have previously been mixed. Shake well. NOTE: Dispense with a "shake well" label.

A useful book in the field of veterinary preparations is *Practical Veterinary Pharmacology, Materia Medica and Therapeutics* by H. J. Milks (1940), published by Alexander Eger, Chicago. This is a typical pharmacology text, which lists preparations and discusses their actions. It is not a formula book but does contain many prescriptions and lists other veterinary preparations for which formulas can be found in the standard reference books. There is also a British volume, *Veterinary Counter Practice* (1937), which was published by Chemist and Druggist, 28 Essex Street, London, W. C. 2. Although this is a formula book, it contains a number of things peculiar to British pharmacy and veterinary practice which may reduce its usefulness somewhat in this country.

PEROXIDES DEVELOP IN OIL

I have prepared 1% ephedrine in light mineral oil with the addition of a small amount of oleic acid. The solution is very clear but has developed a slight yellow color and a disagreeable odor after two months' standing. Can I overcome the odor in any way and still use the above formula?—T. R., Fla.

It would not seem to be possible to eliminate the odor from the preparation which has already been made. But it should be quite possible to prepare additional material satisfactorily, provided that the ingredients are carefully selected. As ephedrine is sufficiently soluble in light mineral oil to give the 1% solution, the use of oleic acid would not seem to be necessary. Oleic acid definitely is responsible for part of the yellow color which develops and quite possibly also aids in developing the disagreeable odor.

Considerable evidence has been submitted to show that the disagreeable odor is primarily due to the development of peroxides in the liquid petrolatum. Both moisture and light will bring about the development of these peroxides. In Ephedrine Nebula the National Formulary specifies "light liquid petrolatum rendered anhydrous but not heated at a temperature above 40° C." The liquid petrolatum itself, as well as the ephedrine solution itself, should be kept in a dark place.

The Hospital Pharmacist

Plans for Developing
BETTER PROFESSIONAL RELATIONS

by SISTER MARY OSWALDA

SAINT JOSEPH'S CHILDREN'S AND MATERNITY HOSPITAL, SCRANTON, PA.

EIGHT-POINT PROGRAM GIVEN FOR BROADENING USEFULNESS AND INCREASING RECOGNITION OF THE HOSPITAL PHARMACIST

BETTER professional relations, increased opportunities, and a large measure of satisfaction will come to the hospital pharamcist who goes beyond the routine duty of dispensing drugs and medical supplies to develop and operate a well-planned pharmaceutical service. Eight projects are outlined—and others could be developed—which, in their execution, will throw into bold relief the place of professional pharmacy in the mosaic of a complete hospital health service.

First of all the pharmacy should be arranged to be practical as well as artistic. Stock should be well classified according to the system best suited to individual needs, for example, by arranging preparations according to their classifications, such as hypnotics, analgesics, diuretics, cough medicines, cathartics, dermatological pastes, ointments, vitamins, etc., or placing products in alphabetical arrangement on the shelves. Very potent or poisonous products should, of course, be in a cabinet by themselves. It is understood that all biologicals and medicinal syrups, Cod-Liver Oil, Nitroglycerin, Spirit of Nitrous Ether, Ethyl Chloride, etc., will always be kept in the refrigerator. No food or beverages should be kept there, except perhaps carbonated water.

Definite rules may be printed, framed and hung up at the nurses' station on each floor and in various departments. These should specify the hours the pharmacy will be open and the hours when requisitions for drugs will be filled, for example, the time in the morning when "stock" preparations and special or individual prescriptions are to be brought for refills. There should be directions for the proper placing and screwing of caps on the containers, and proper cautions regarding medicines. For instance, nurses may be warned to read the label on the bottle at least three times before administering the preparation to the patient. Secondly, no medicine should be removed from the original container and labeled by the nurse, and retained in the medicine cabinet while she sends the original container to the pharmacy to be refilled.

A poison chart with the antidotes covering all the stock and special preparations used in your hospital should be hung close to the medicine cabinet in each department. A special medicine cabinet containing proper antidotes placed near the regular medicine cabinet permits prompt handling of emergencies in case an overdose or wrong medicine is administered to a patient.

A third objective is the manufacturing of phar-

maceutical products. A hospital pharmacist should manufacture practically all of the U. S. P. and N. F. preparations and others found in the Pharmaceutical Recipe Book—especially ointments and pastes, syrups, liniments, liquors, elixirs, many of the fluidextracts, and tinctures.

A hospital pharmacist obviously can manufacture preparations containing alcohol at a very marked saving to the institution. A statement should be prepared in triplicate form which tabulates the preparations manufactured during the month. Under each heading is written the date, name of preparation, quantity manufactured and the actual cost. In an adjoining column is listed the amount it would cost if purchased from a manufacturer or wholesaler. The number of prescriptions compounded and their cost as against the cost if compounded in the retail drug store can also be included.

One copy of this report should be presented to the superintendent each month, one to the board of directors, and one retained by the pharmacist. In this way the pharmacist is able to prove his worth and service to the hospital.

As a fourth objective a hospital formulary should be established to promote the use of preparations of the U. S. P. and N. F. and the Pharmaceutical Recipe Book by staff physicians, and to discourage the use of any proprietary medicines which fall short of their claims or duplicate official products.

If we were to stock all the various hypnotic and cardiac preparations under proprietary names that physicians might wish to prescribe, not to mention many others, thousands of dollars would be tied up in "dead stock" at the end of each year thus hindering the pharmaceutical service of the hospital.

Establishing a Formulary

To establish a hospital formulary, it will be necessary to select a hospital formulary committee. This can be effected best by appointment of the chief doctor from each of the special fields, such as the dermatologist, gynecologist, cardiac specialist, gastro-enterologist, pediatrician, etc. These doctors should be held to definite printed rules, such as (1) prescribing the official U. S. P. and N. F. preparations whenever possible; (2) not admitting any proprietary product to the formulary if the individual medicaments can be obtained and economically compounded by the pharmacist to produce the desired effect; (3) admitting no product of unknown composition; (4) avoiding adoption of the so-called specialties, such as some of the ampul products for hypodermic, intramuscular or intravenous use, unless they have been accepted by the American Medical Association's Council on Pharmacy and Chemistry; (5) encouraging the oral route of administration when the effect can be obtained without giving the drug intravenously.

Revised Regularly

A hospital formulary of this type is now being completed for use in our own hospital. It will be in loose-leaf style so that new formulas of interest to the physicians can be printed on paper of the same dimensions as the formulary and inserted under their proper classifications. A photograph of the torsion balance will also be included with a caption reading: "Doctor, this is the torsion balance used in weighing the more potent drugs for your prescriptions." A photograph showing the interior of the biological refrigerator will be captioned, "Doctor, in this refrigerator is stored the biologicals, diphtheria and tetanus antitoxin, insulin, medicinal syrups, etc." A photograph of the distiller with an appropriate notation underneath, as well as one of the reference library, will also be used.

A 20- by 30-inch card listing the drugs under the same classifications as used in the formulary will be hung at the nurses' station on each floor where the doctors come to write their prescriptions.

A fifth objective is the teaching of materia medica to nurses, for the pharmacist is usually well prepared to teach this subject. Specimens of the drugs that are to be discussed should be taken to the classroom. In the case of vegetable or botanical drugs, the pharmacist should take the crude drug and all its different preparations and explain the difference in potency of the doses of each. Chemotherapeutic agents are similarly handled, thus making the subject more alive and interesting to the nurses.

The sixth objective is to assist the physicians in their prescription writing by giving them the benefit of the pharmacist's knowledge of incompatibilities, proper use of vehicles, and informa-

tion on other problems involved. This can be effected by attending staff meetings or calling a special meeting three or four times a year. Be sure to use a demonstration board on such occasions for writing the prescriptions. At this time formulas can also be distributed to be slipped into the loose-leaf style hospital formulary. We should make it a point to copy formulas that appear in our own *Journal of the American Pharmaceutical Association*. Reference notations should be included. For example, the formulas recently published for treating fungus infections would be marked: "This formula was taken from the *Journal of the American Pharmaceutical Association* (Practical Pharmacy Edition), Vol. IV, No. 4."

A seventh objective is having pharmaceutical exhibits, not only during the observance of National Pharmacy Week, but at least four or five times a year. A cabinet can be placed in the physicians' consultation room and used for pharmaceutical displays, such as a collection of official vehicles, botanicals, ointments for fungus infections, or preparations for diabetic patients.

The eighth objective is giving publicity outside of the hospital itself to pharmacy's professional character.

For instance, a pharmacy exhibit can be placed in a prominent store window during National Pharmacy Week.

Whenever there are pharmaceutical exhibits either in a store window or in the hospital they should be publicized by radio announcements and by inviting the attendance of science students of local high schools or near-by colleges. Permission may also be obtained to give science students a lecture once or twice a year on some timely phase of pharamcy. In this way, we can increase interest in pharmacy as a profession, emphasize its services, and develop professional relations with our co-workers in related fields.

Presented by title to American Society of Hospital Pharmacists, A. PH. A., Columbus meeting, 1943.

APPLICATION FOR MEMBERSHIP

American Pharmaceutical Association

Approving of its objectives, I hereby apply for active membership in the American Pharmaceutical Association and subscribe to the "Journal of the American Pharmaceutical Association." Enclosed is $____ for membership dues with subscription to the ☐ Practical Pharmacy Edition at $5; ☐ Scientific Edition at $6; ☐ Both Editions at $7.

Name in Full_____

Number and Street_____

Town_____ **State**_____

Graduate of_____ **Year**_____ **Degrees**_____

I am a registered pharmacist in _____ and am engaged or, in the case of retirement, was engaged as: __ Retailer, __ Wholesaler, __ Manufacturer, __ Drug Importer, __ Teacher, school official or librarian, __ Research Worker, __ Editor, __ Publisher, __ Representative, __ Pharmaceutical Chemist, __ Food and Drug Official, __ Hospital Pharmacist, __ Association Official, __ Pharmacist in Government Service, __ Student.

The applicant named above is recommended by the undersigned two members:

Name_____ **Name**_____

If the applicant is unacquainted with any member of the Association, the officers will aid in securing the necessary recommendations. This application, with the payment of dues for one year, may be sent to any member of the membership committee, the Secretary, or any officer of the Association.

Date_____ **E. F. KELLY, *Secretary*, 2215 Constitution Avenue, Washington 7, D. C.**

ACTIVITIES OF A. PH. A. BRANCHES

NOMINATIONS have been made for the 1944 Remington medal award, Dr. Hugo Schaefer reported at the March meeting of the New York branch. Fifty-five persons were present at the meeting to hear Dr. Marvin R. Thompson, president of Wm. R. Warner & Company, discuss the possible relationship between certain detoxicants and diseases with cardiovascular-renal involvement. Later the members were told of the reported loss of Dr. E. F. Kelly's son in a bombing mission over Germany, and it was directed that a letter of condolence be sent to the A. PH. A. secretary.

Pharmacy and the public health was the theme of the April meeting of the New York branch, which was held at the College of Pharmacy, Fordham University. "The Hospital Pharmacist's Role in Public Health" was discussed by Miss Mary Grace, chief pharmacist of Lincoln Hospital. Dr. C. R. Addinall of the Merck Research Laboratory spoke on "The Pharmaceutical Manufacturer's Contribution to Public Health and the War Effort." As executive director of the American Social Hygiene Association, Dr. Walter Clarke addressed the group on "The Pharmacist's Part in the Social Hygiene Program." Dr. Ivor Griffith, president of the AMERICAN PHARMACEUTICAL ASSOCIATION, discussed "The Retail Pharmacist's Part in Public Health and the War Effort." Members of the various pharmaceutical associations of the metropolitan area and the alumni of the Fordham pharmacy college were invited to attend this meeting.

Principal speaker at the meeting of the Philadelphia branch was Dr. Melvin Green of the AMERICAN PHARMACEUTICAL ASSOCIATION laboratory. He reported on the various A. PH. A. activities as well as the work of its laboratory. Considerable laboratory work directly related to the war effort has been done in addition to the development of new drug standards.

At the joint meeting of the A. PH. A. student branch and the Academy of Science at Fordham University, Dr. Ralph Clark of Merck & Company spoke on "Wartime Pharmacy," candidly discussing current problems and the future of pharmacy.

Fifty-seven were in attendance at the last meeting of the Northwestern branch to hear Dr. Charles A. Mann, chief of the Division of Chemical Engineering, University of Minnesota, speak on "Plastics, Their Present and Post-War Uses."

Volatile Oil Seminar

Members of the Ohio State student branch recently held a volatile oil seminar. Miss Marian Adams discussed some of the plants indigenous to the United States that bear volatile oils and the methods of preparing oils from them. The oil-bearing plants that grow in French Morocco were discussed by Jack E. Scott. Miss Mary Kembinsky spoke on Hungarian oils. Olus Scott Swank told the members about the volatile oils of Kenya. Dr. B. V. Christensen, dean of the college, summarized the subject and explained why some of the volatile oils cannot be successfully produced in this county. He pointed out that some standards are being changed to make possible the use of more of our native plants.

At the March meeting of the University of Mississippi student branch, Byron Gathright, a local pharmacist, spoke on "Requirements of a Pharmacist." A week later the members gathered at the "Tea Hound" for their annual banquet.

New officers at the Temple University student

1821 1944

What of TOMORROW? The future of Pharmacy rests with young women and men educated thoroughly and practically. Entering classes begin Oct. 30, 1944 for accredited courses leading to B.Sc. degrees in Pharm., Chem., Bact. or Biol. in little less than 3 years. Write for catalog.

Inquiries invited from returning service men.

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COLLEGE OF PHARMACY AND SCIENCE

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branch are Charles S. Kumkumian, president; Theodore J. Drygas, vice-president; Faye M. Miller, secretary; and Blaine W. Miller, treasurer.

Officers elected for the student branch at the College of Pharmacy, Howard University, are Amos G. Cranford, president; Kermit H. McNair, vice-president; Simuel J. Garret, treasurer; and Kenneth W. Richardson, secretary.

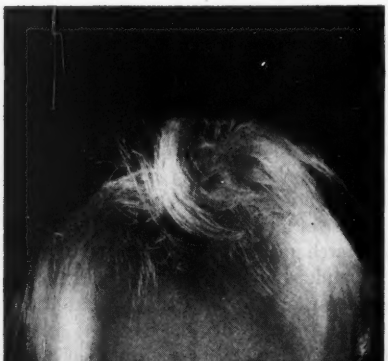
Dr. Curt P. Wimmer addressed the March meeting of the student branch at Columbia University. His discussion of "The Use of Ultra-Violet Rays in Pharmacy" was followed by laboratory demonstrations. About 15 of the student members later attended the meeting of the New York branch. New officers of the student branch are David Frolich, president; Bernaid Bartner, vice-president; Roland Weisenfield, treasurer; and Eleanor Stark, secretary.

At the joint meeting of the Western New York branch and the University of Buffalo student branch, Dr. Ivan Bunnell of the Meyer Memorial Hospital reported on two cases of serious bromide poisoning. Due to excessive worry, the patients had, for several weeks, resorted to large doses of bromide salts for sedation. The treatment of replacing the bromide ion in the blood with the chloride ion resulted in recovery after several weeks. The second speaker was Francis Sturner, pharmacist at Buffalo General Hospital, who outlined the functions of a hospital pharmacy and discussed the advantages of institutional practice. A discussion period followed, led by Ralph W. Engelhardt, pharmacist at Rochester State Hospital.

New officers at the University of Colorado student branch are Russel Morgey, president; Clark Kelly, vice-president; Donna Mae Roy, secretary; and Martha Shoup, treasurer. At the March meeting each member was presented with a copy of the A. PH. A. constitution.

PHARMACY WEEK COMMITTEE NAMED; OBSERVANCE DATE SET

National Pharmacy Week for 1944 has been designated as November 5 through November 11 and program plans are getting under way with the appointment of the official committee to



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1. National Formulary, Seventh Edition, 1942, Page 316.
2. Symposium on Pectin & Pectin Pastes, Bulletin of the National Formulary Committee, Vol. 9, No. 1, Oct. 1940.

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direct the activities. Members of the new Committee on Pharmacy Week announced by the AMERICAN PHARMACEUTICAL ASSOCIATION are:

A. Lee Adams, 209 Park Avenue, Glencoe, Illinois (N.A.R.D.); A. R. Granito, 30 Martin Terrace, Hackensack, New Jersey (N.A.R.D.); Emil C. Horn, 4505 West Burleigh St., Milwaukee, Wisconsin (N.A.R.D.); Harold V. Darnell, 710 Test Bldg., Indianapolis, Indiana; Llewellyn L. Eisentraut, Hardin Road & Mondamin, Des Moines, Iowa; Leonard J. Dueker, 2028 Adelaide Avenue, St. Louis, Missouri; Bernard A. Bialk, 11655 Hamilton at Webb, Detroit, Michigan; Ralph Bienfang, College of Pharmacy, University of Oklahoma, Norman, Oklahoma; Edward A. Hay, 439 Cumberland, Portland, Maine; Julian W. Holt, Meridian, Mississippi; E. W. Gibbs, 1029 South 20th, Birmingham, Alabama; Walter Rhodes, 6316 North Minnesota Avenue, Portland, Oregon; Louis J. Fischl, 411 30th Street, Oakland, California; C. R. Bohrer, Chairman, 2215 Constitution Avenue, N. W., Washington, D. C.

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Guava powder, obtained from the fruits of a neglected tropical shrub, is now being used by British troops as a rich source of vitamin C, and research in the United States indicates that pharmacists may soon hear more about the product, a Science Service report states.

Dried guava is so rich in vitamin C that a little over four ounces would protect an Arctic explorer from scurvy for almost three months. In the forthcoming *Handbook of Nutrition*, Dr. Russell M. Wilder and Thomas E. Keys of the Mayo Clinic point out that the powder is reputed to contain a "rather phenomenal quantity of ascorbic acid, 2500 to 3000 milligrams per 100 grams," according to research reports from South African laboratories. The product is pleasantly aromatic but has little taste.

Vitamin C was found to be at the high level of 2.5% to 3%, even exceeding such rich sources as dried rose hips, which are reported to contain about 2%.

ELECTRON MICROANALYZER IDENTIFIES VIRUS ELEMENTS

Chemical elements composing such extremely minute submicroscopic objects as the tail or head of a bacterium or a virus, can be identified in a few minutes by a new instrument, the electron microanalyzer, developed by Dr. James Hillier of RCA Laboratories.

As a running mate to the electron microscope, the new instrument will allow the determination of the composition as well as the size, shape and internal structure of the particles which a few years ago were quite beyond the most powerful means of exploration in the microscopic world.

In the electron microanalyzer a very small area of the specimen is irradiated with a electron probe, a stream of these particles of electricity brought into a beam by a two-stage magnetic lens system. The electrons transmitted by the irradiated area of the specimen are focused by a third magnetic lens so that the electron probe is reformed. The amount of energy lost by the electrons is measured through a photographic exposure, and the position of markings in the electron velocity distribution indicates the presence of a chemical element in the specimen.

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THROMBOTIC ILLS RESPOND TO SYNTHETIC DICUMAROL

Effectiveness of synthetic dicumarol as an anticoagulant in certain indications, particularly thrombophlebitis, is further established in a report by Lt. Howard D. Zucker, (MC) U.S.N.R. (*Jour. Am. Med. Assoc.*, 124: 217, 1944).

Dicumarol was administered orally to a small series of 18 patients where some type of blood clotting was either present or seemed likely. All had uncomplicated recoveries. Nine of the patients had blood clot in the lower extremities in conjunction with inflammation of the vein wall, known as thrombophlebitis. The treatment also seemed to have a beneficial effect in cases of thrombosis and embolism. Lt. Zucker feels that dicumarol may ultimately find a place in the prevention of thrombosis and embolism and in the treatment of thrombophlebitis.

The new drug may prove to be a popular one for these conditions because of its cheapness and ease of administration, if further clinical trials confirm its value.

In the cases reported, an initial dose of 300 mg. of dicumarol by mouth was given, followed by 200 mg. the following morning. Subsequent doses were given with the aim of maintaining the plasma prothrombin level between 60% and 30% of normal. Lt. Zucker emphasizes the importance of the slope of the plotted prothrombin curve in determining dosage. The average duration of treatment of the thrombophlebitis cases was 14 days. Liver damage or renal impairment contraindicates the use of dicumarol.

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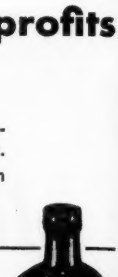

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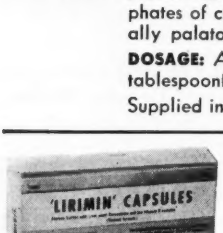
Supplied in pint and gallon bottles.



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Committee on Recipe Book.—*Chairman*, Melvin W. Green, Washington, D. C. (1949); G. C. Schicks, Newark, N. J. (1944); R. E. Terry, Chicago, Ill. (1945); M. A. Chehak, Cedar Rapids, Iowa (1946); F. S. McGinnis, Pittsburgh, Pa. (1947); F. D. Lascoff, New York City (1948); F. E. Bibbins, Indianapolis, Ind. (1949).

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Appointed by the President

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Committee on Legislation.—*Chairman*, A. L. I. Winne, Richmond, Va.; R. P. Fischelis, Trenton, N. J.; H. H. Schaefer, Brooklyn, N. Y.; A. G. DuMez, Baltimore, Md.; E. F. Kelly, Washington, D. C.; C. Leonard O'Connell, Pittsburgh, Pa.; Geo. H. Frates, Washington, D. C.

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Madison, Wis. (1948). (This Committee is a part of the National Committee on Pharmaceutical Syllabus, the other members being appointed by the A. A. C. P. and the N. A. B. P.)

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American Association for the Advancement of Science.—*Councilors*, E. F. Kelly, Washington, D. C.; G. L. Jenkins, Lafayette, Ind.; J. A. Reese, Lawrence, Kan.

National Drug Trade Conference Delegates.—G. D. Beal, Pittsburgh, Pa. (1945); E. F. Kelly, Washington, D. C. (1946); R. P. Fischelis, Trenton, N. J. (1944).

PREPARATION OF ISOTONIC SOLUTIONS

Have you read Dr. J. M. Wells comprehensive discussion of the preparation of isotonic solutions beginning on page 99 of THIS JOURNAL? If you desire copies of this time-saving material for use in your prescription laboratory or to give to other pharmacists, send requests with ten cents for each reprint to the editor at 2215 Constitution Ave., Washington 7, D. C.

branch are Charles S. Kumkumian, president; Theodore J. Drygas, vice-president; Faye M. Miller, secretary; and Blaine W. Miller, treasurer.

Officers elected for the student branch at the College of Pharmacy, Howard University, are Amos G. Cranford, president; Kermit H. McNair, vice-president; Simuel J. Garret, treasurer; and Kenneth W. Richardson, secretary.

Dr. Curt P. Wimmer addressed the March meeting of the student branch at Columbia University. His discussion of "The Use of Ultra-Violet Rays in Pharmacy" was followed by laboratory demonstrations. About 15 of the student members later attended the meeting of the New York branch. New officers of the student branch are David Frolich, president; Bernard Bartner, vice-president; Roland Weisenfield, treasurer; and Eleanor Stark, secretary.

At the joint meeting of the Western New York branch and the University of Buffalo student branch, Dr. Ivan Bunnell of the Meyer Memorial Hospital reported on two cases of serious bromide poisoning. Due to excessive worry, the patients had, for several weeks, resorted to large doses of bromide salts for sedation. The treatment of replacing the bromide ion in the blood with the chloride ion resulted in recovery after several weeks. The second speaker was Francis Sturner, pharmacist at Buffalo General Hospital, who outlined the functions of a hospital pharmacy and discussed the advantages of institutional practice. A discussion period followed, led by Ralph W. Engelhardt, pharmacist at Rochester State Hospital.

New officers at the University of Colorado student branch are Russel Morgey, president; Clark Kelly, vice-president; Donna Mae Roy, secretary; and Martha Shoup, treasurer. At the March meeting each member was presented with a copy of the A. PH. A. constitution.

PHARMACY WEEK COMMITTEE NAMED; OBSERVANCE DATE SET

National Pharmacy Week for 1944 has been designated as November 5 through November 11 and program plans are getting under way with the appointment of the official committee to

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direct the activities. Members of the new Committee on Pharmacy Week announced by the AMERICAN PHARMACEUTICAL ASSOCIATION are:

A. Lee Adams, 209 Park Avenue, Glencoe, Illinois (N.A.R.D.); A. R. Granito, 36 Martin Terrace, Hackensack, New Jersey (N.A.R.D.); Emil C. Horn, 4505 West Burleigh St., Milwaukee, Wisconsin (N.A.R.D.); Harold V. Darnell, 710 Test Bldg., Indianapolis, Indiana; Llewellyn L. Eisentraut, Hardin Road & Mondamin, Des Moines, Iowa; Leonard J. Dueker, 2028 Adelaide Avenue, St. Louis, Missouri; Bernard A. Bialk, 11655 Hamilton at Webb, Detroit, Michigan; Ralph Bienfang, College of Pharmacy, University of Oklahoma, Norman, Oklahoma; Edward A. Hay, 439 Cumberland, Portland, Maine; Julian W. Holt, Meridian, Mississippi; E. W. Gibbs, 1029 South 20th, Birmingham, Alabama; Walter Rhodes, 6316 North Minnesota Avenue, Portland, Oregon; Louis J. Fischl, 411 30th Street, Oakland, California; C. R. Bohrer, Chairman, 2215 Constitution Avenue, N. W., Washington, D. C.

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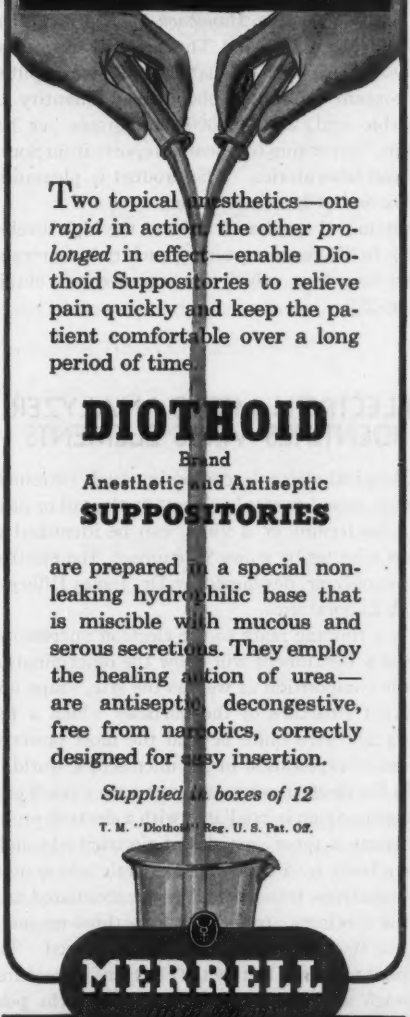

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GUAVA BECOMES POPULAR AS SOURCE OF VITAMIN C

Guava powder, obtained from the fruits of a neglected tropical shrub, is now being used by British troops as a rich source of vitamin C, and research in the United States indicates that pharmacists may soon hear more about the product, a Science Service report states.

Dried guava is so rich in vitamin C that a little over four ounces would protect an Arctic explorer from scurvy for almost three months. In the forthcoming *Handbook of Nutrition*, Dr. Russell M. Wilder and Thomas E. Keys of the Mayo Clinic point out that the powder is reputed to contain a "rather phenomenal quantity of ascorbic acid, 2500 to 3000 milligrams per 100 grams," according to research reports from South African laboratories. The product is pleasantly aromatic but has little taste.

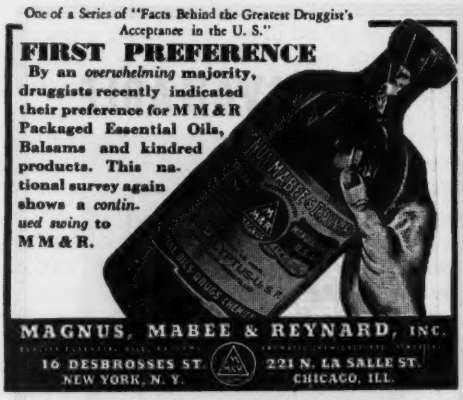
Vitamin C was found to be at the high level of 2.5% to 3%, even exceeding such rich sources as dried rose hips, which are reported to contain about 2%.

ELECTRON MICROANALYZER IDENTIFIES VIRUS ELEMENTS

Chemical elements composing such extremely minute submicroscopic objects as the tail or head of a bacterium or a virus, can be identified in a few minutes by a new instrument, the electron microanalyzer, developed by Dr. James Hillier of RCA Laboratories.

As a running mate to the electron microscope, the new instrument will allow the determination of the composition as well as the size, shape and internal structure of the particles which a few years ago were quite beyond the most powerful means of exploration in the microscopic world.

In the electron microanalyzer a very small area of the specimen is irradiated with a electron probe, a stream of these particles of electricity brought into a beam by a two-stage magnetic lens system. The electrons transmitted by the irradiated area of the specimen are focused by a third magnetic lens so that the electron probe is reformed. The amount of energy lost by the electrons is measured through a photographic exposure, and the position of markings in the electron velocity distribution indicates the presence of a chemical element in the specimen.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THROMBOTIC ILLS RESPOND TO SYNTHETIC DICUMAROL

Effectiveness of synthetic dicumarol as an anticoagulent in certain indications, particularly thrombophlebitis, is further established in a report by Lt. Howard D. Zucker, (MC) U.S.N.R. (*Jour. Am. Med. Assoc.*, 124: 217, 1944).

Dicumarol was administered orally to a small series of 18 patients where some type of blood clotting was either present or seemed likely. All had uncomplicated recoveries. Nine of the patients had blood clot in the lower extremities in conjunction with inflammation of the vein wall, known as thrombophlebitis. The treatment also seemed to have a beneficial effect in cases of thrombosis and embolism. Lt. Zucker feels that dicumarol may ultimately find a place in the prevention of thrombosis and embolism and in the treatment of thrombophlebitis.

The new drug may prove to be a popular one for these conditions because of its cheapness and ease of administration, if further clinical trials confirm its value.

In the cases reported, an initial dose of 300 mg. of dicumarol by mouth was given, followed by 200 mg. the following morning. Subsequent doses were given with the aim of maintaining the plasma prothrombin level between 60% and 30% of normal. Lt. Zucker emphasizes the importance of the slope of the plotted prothrombin curve in determining dosage. The average duration of treatment of the thrombophlebitis cases was 14 days. Liver damage or renal impairment contraindicates the use of dicumarol.